

## Discovery Cohort Update

The Discovery cohort continues to assess people with Parkinson's (PwP) every 18 months in face-to-face clinics. Sadly, as the cohort ages some of our participants have passed away or have had to withdraw due to advancing frailty. We recognise these difficulties, and therefore have developed a shorter assessment that can be done on the telephone for PwP who find coming to clinic difficult. We also refund necessary travel expenses, including taxi services to help where needed. Most PwP in our cohort have now been seen over a minimum of 3 years, i.e. at baseline, 18 and 36 month visits. We are now applying for further funding from Parkinson's UK to extend this follow up for another 5 years, ensuring that as many PwP as possible can be reviewed for up to 10 years from diagnosis.

Successful renewal of Discovery funding from 2020 to 2025 will ensure that we can:

1. Evaluate the health, economic and personal costs of Parkinson's
2. Test our new sleep study wearable kit across PwP, RBD and control participants
3. Continue to evaluate the motor smartphone test in monitoring Parkinson's
4. Deliver two clinical trials aimed at slowing down the progression of Parkinson's.



**OPDC Clinical team:** (L to R) Sam Evetts, Christine Lo, Francesca Bowring, Jane Rumbold, Michele Hu, Johannes Klein, Marie Crabbe, Katie Ahmed, Tom Barber, Claire El Mouden



- New study looks at sleep and its link to Parkinson's
- Our smartphone project is helping us better monitor and detect Parkinson's and RBD
- Brain imaging research sheds light on apathy in RBD
- Using statistics to better understand Parkinson's
  - A common variant in genomes and its effect on Parkinson's risk
- Parkinson's UK Oxford Branch news

## ABOUT OPDC

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## Redefining priorities for Parkinson's research

In 2014, the James Lind Alliance (JLA) and Parkinson's UK set up a Patient Setting Priority group to identify the top 10 research priorities that people living with Parkinson's and health and social care professionals would like to see answered. At the 2016 OPDC open day we asked our study participants for their priorities. These differed from those found in the JLA/Parkinson's UK 2014 survey, and included issues related to speech problems and therapies. We would now like to update this survey and also extend the survey to those taking part in Parkinson's research across Europe.

If you would like to take part in this survey or would like more information please visit <https://tinyurl.com/centrepdtop10> or contact Francesca Bowring on 01865 234 769 / [Francesca.Bowring@nhs.net](mailto:Francesca.Bowring@nhs.net)

## Major new study launched to investigate the link between sleep problems and Parkinson's

Researchers at OPDC are embarking on a new five-year study looking at the links between a condition known as Rapid Eye Movement Sleep Behaviour Disorder (RBD) and Parkinson's. Funded by the NIHR Oxford Biomedical Research Centre, the study seeks to improve the remote diagnosis and monitoring of sleep problems at home.

RBD is a sleep problem where the switch that normally turns off movement during sleep is faulty, causing people to move or shout while asleep. A person who goes on to develop Parkinson's may have RBD for many years before any problem with their movement begins.

The team of researchers, led by OPDC's Michele Hu, will work with Maarten De Vos in the Oxford Institute of Biomedical Engineering to develop computer algorithms that will provide instant diagnosis by processing the data collected from devices worn at home.

*"My first aim is to identify the people with RBD who are at the highest risk of developing Parkinson's before their symptoms appear. If we can do this, it may allow us to start them on treatment to slow down or even prevent the onset of Parkinson's. My second aim is to understand the impact of Parkinson's on sleep quality and whether people with Parkinson's might benefit from treatment to help their sleep."*  
Michele Hu

The first step is to invite people who need an NHS sleep study to wear the new kit at the same time. Having both sets of data will help the team 'train' computer algorithms to correctly interpret the data that the wearable kit collects. The team then hope to recruit people from across the UK who have either RBD or Parkinson's, to wear the sleep monitoring device for a few nights every six months.



For further information about taking part in the study, please email [sleep.wearables@nhs.net](mailto:sleep.wearables@nhs.net).

## Exciting developments with OPDC's smartphone app research – Christine Lo and Siddharth Arora

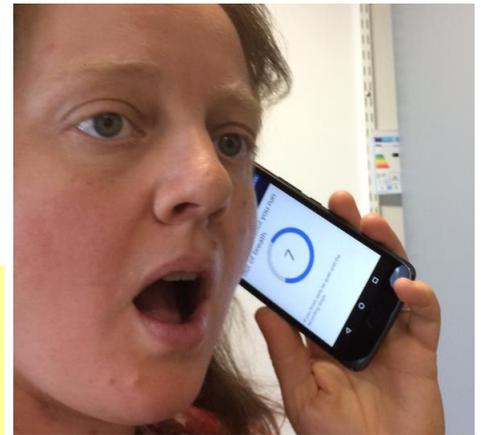
A key priority for the OPDC is to diagnose Parkinson's as early as possible, so people can get treatment sooner. Currently, Parkinson's is diagnosed in-clinic, only when physical symptoms become apparent. However, we know there are changes in the brain 5 to 10 years before any significant physical symptoms appear. An exciting possibility we are investigating is whether smartphones can be used to detect subtle differences in the physical symptoms associated with Parkinson's and REM sleep behaviour disorder (RBD). People with RBD are at significantly higher risk of developing Parkinson's, therefore we want to know if a smartphone can help identify people with either of the two conditions and tell them apart.

The smartphone app features 7 tests to measure voice, balance, walking, finger tapping, reaction time, and rest and postural tremor. Overall, the test takes about eight minutes to perform. We are currently collecting recordings both in-clinic and at-home.

Using the smartphone recordings, we have developed mathematical algorithms that quantify patterns of motor impairment that are specific to RBD, Parkinson's, and healthy controls. We recently published a paper, based on data collected by the Discovery research cohort, whereby we report that smartphones can be used to discriminate between the three participant groups with an 85-92% average accuracy.

To further validate and refine our methodology for detecting and monitoring the motor symptoms of Parkinson's and RBD, we are in the process of collecting additional smartphone recordings. To do this, the OPDC is going to partner with other Parkinson's and RBD research groups around the world. With an aim to make an international roll-out possible, we are very excited to announce the launch of a new smartphone app that will work in thirteen different languages! To coincide with this launch, the University of Oxford's Public Affairs team have made a short film to promote our smartphone app research, which will be available via our website soon.

We are in the process of testing a 'beta' version of the smartphone app, and we need people who would be willing to test it at home for us. If you are interested in helping us, please email: [sleep.wearables@nhs.net](mailto:sleep.wearables@nhs.net).

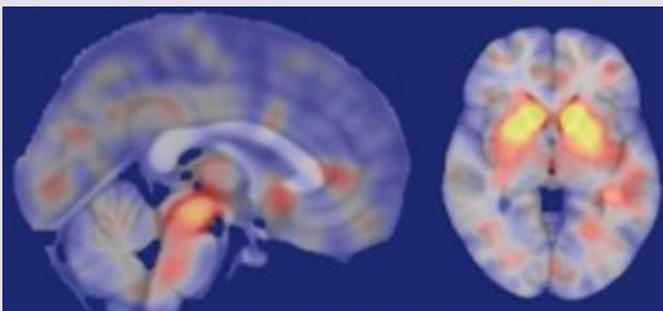


Arora S, Baig F, Lo C, Barber TR, Lawton MA, Zhan A, Rolinski M, Ruffmann C, Klein JC, Rumbold J, Louvel A, Zaiwalla Z, Lennox G, Quinnell T, Dennis G, Wade-Martins R, Ben-Shlomo Y, Little MA, Hu MT. (2018) Smartphone motor testing to distinguish idiopathic REM sleep behavior disorder, controls, and PD. *Neurology*. PMID:30232246

## Apathy in REM sleep behaviour disorder – Tom Barber

Last year, we published a paper showing that apathy is very common in people with idiopathic REM sleep behaviour disorder (RBD), and we have now followed this up with a brain imaging study that sheds light on the reasons for this.

Apathy is a condition where people feel a sense of indifference to doing activities or being with other people. It is very common in people with Parkinson's and can severely affect their lives and those of their friends and family. Although apathy often occurs with depression, the two conditions are distinct and may require different treatments. We recently showed that nearly half of patients with RBD have some degree of clinical apathy – interestingly, this is even higher than in patients with Parkinson's, suggesting there may be a link between RBD itself and apathy.



To find out more, we performed MRI and DAT scans in 43 patients with RBD. DAT scans can measure the levels of dopamine and serotonin in the brain, two important chemicals that are affected by Parkinson's. Because people with RBD have a high risk of developing Parkinson's in the future, we wanted to investigate whether the level of these chemicals is already affected. We found that although some patients had reduced levels of dopamine in the brain, it was low levels of

serotonin that were related to apathy. The region where the serotonin level was measured (an area of the brain called the dorsal raphe nucleus) is very close to the region that is involved in the causation of RBD, which may explain why people with RBD have a high rate of apathy.

Next, we plan to find out whether the same link between apathy and low serotonin levels is present in people with Parkinson's, and if so, whether medications that increase serotonin availability in the brain might improve symptoms of apathy.

Barber TR, Griffanti L, Muhammed K, Drew DS, Bradley KM, McGowan DR, Crabbe M, Lo C, Mackay CE, Husain M, Hu MT, Klein JC; Oxford Parkinson's Disease Centre. (2018) Apathy in rapid eye movement sleep behaviour disorder is associated with serotonin depletion in the dorsal raphe nucleus. *Brain*. PMID:30212839.

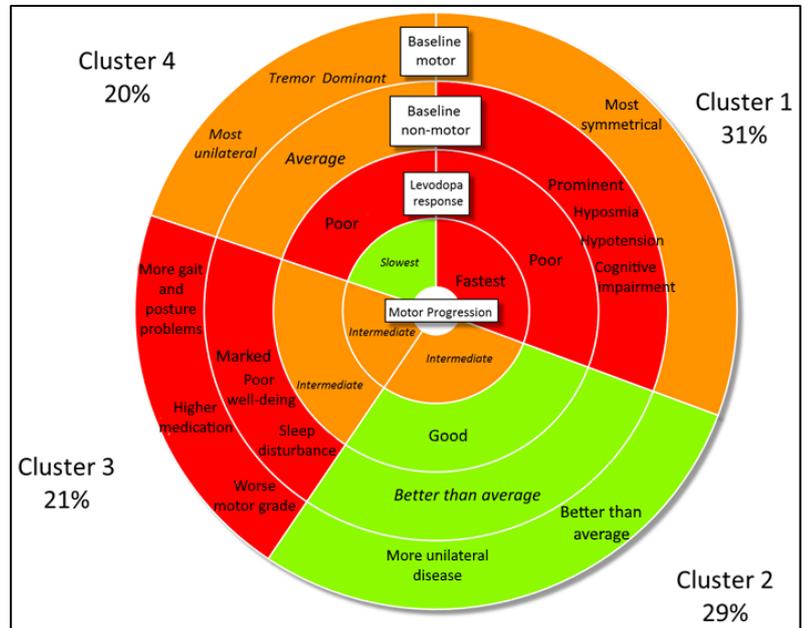
# Defining Parkinson's Subtypes – Michael Lawton

Just as every person is unique, every person with Parkinson's presents with a different range of symptoms at varying severities. These differences (referred to as "heterogeneity"), have led many clinicians to believe that there are different subtypes of Parkinson's. We have tried to answer this question using the OPDC Discovery cohort and another UK Parkinson's Disease cohort called the Tracking Parkinson's cohort.

A statistical technique called "k-means cluster analysis" segregated people into subtypes based on motor and non-motor symptoms at their baseline assessment. Whereas Dr Who and the TARDIS worked in 5 dimensions in the TV series, we had to work in many more dimensions for our model and we found four subtypes that replicated well across the two cohorts.

The most interesting result is that these four subtypes seem to differ in response to levodopa and that one subtype progresses faster in motor disability than the others. We have started to consider whether genetic and blood serum biomarkers might be related to these subtypes and initial results look very promising.

The next stage in our analyses plans are to try and replicate our findings in more cohorts of people with Parkinson's worldwide and hope that our results might help inform clinical trials into new medications.



Lawton, M. et al. (2018) Developing and validating Parkinson's Disease subtypes and their motor and cognitive progression. *Journal of Neurology, Neurosurgery and Psychiatry*. doi:10.1136/jnnp-2018-318337

## OPDC welcomes Participants to 2018 Open Day

On September 10th, 2018 over 200 members of Discovery cohort came to the Jury's Inn, Oxford to hear about our latest research and share their views. We would like to thank all of the cohort members who travelled to the event from our centres across the country, and joined in the lively discussion session.

Researchers from across OPDC's themes shared their work. These included talks on our work to develop a new test for Parkinson's based on a key protein (alpha-synuclein), and how we are using skin biopsy samples from our cohort to look for new potential therapies and new drugs trials on our horizon. The programme included our work with wearable technology to better understand Parkinson's and sleep (pages 2-3), how we are working with other large studies of people with Parkinson's to better define Parkinson's (above), and our work on dyskinesia. We also learnt about a new survey to define top priorities for Parkinson's research (page 1) and heard more about the brain donation process. All talks from the open day were filmed and are available to watch at <https://www.opdc.ox.ac.uk/videos>



## Dr Teresa Delgado-Goni and Dr Camille Loiseau join OPDC



Dr Teresa Delgado-Goni is interested in imaging as a valuable tool for the diagnosis, new potential target identification and response to treatment detection in neurodegeneration.

Her aim now is to apply her imaging skills to the development of MRI and molecular imaging protocols using positron emission tomography (PET) to study the symptoms in transgenic models that mimic human Parkinson's.

Dr Camille Loiseau has joined us as a Postdoctoral Neuroscientist to work with Professor Pete Magill.



Camille will be defining how the activity dynamics of basal ganglia neurons are perturbed in Parkinsonism, using a combination of *in vivo* electrophysiological recordings, cell-type-selective manipulations, quantitative neuroanatomy, and behavioural analyses.

## Study investigates how one common variant in genetics can increase the risk of sporadic Parkinson's – Joel BeEVERS

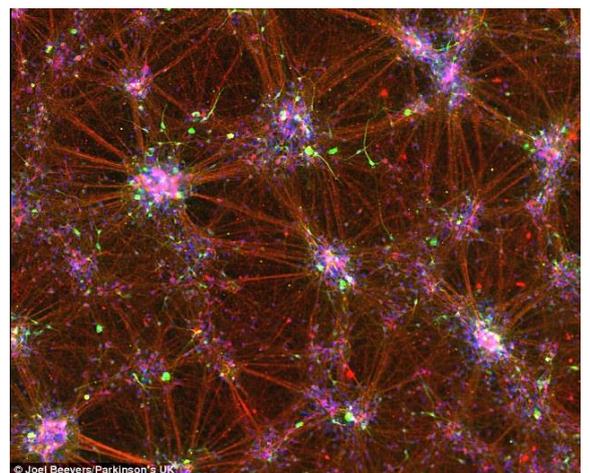
Research from a DPhil project supported by the Oxford branch of Parkinson's UK, has been published in the journal *Stem Cell Reports*. The study, carried out under the supervision of OPDC's Richard Wade-Martins, focused on the microtubule-associated protein tau (MAPT) gene, which provides the code for a set of six proteins called 'tau'. Each of these six tau proteins is made from a different messenger RNA transcript made from the MAPT gene. Of the two normal versions of the MAPT gene, one is overrepresented in people with Parkinson's.

We looked at how small differences between the two normal versions of the MAPT gene change the way the MAPT gene makes the six messenger RNA transcripts and six tau proteins. We found that the version of the MAPT gene that is overrepresented in Parkinson's drives the production of more messenger RNA transcripts overall than the other version of the gene. It also makes different amounts of some of the six specific messenger RNA transcripts.

We then investigated what the function of those specific transcripts may be in the brain cells that die in Parkinson's (dopaminergic neurons), to try and understand how the common genetic differences in MAPT could affect the way neurons function. Using skin cells from human donors to generate stem cells that keep multiplying, we turned them into dopaminergic neurons to study their behaviour.

The different tau proteins had varying effects on transportation within neurons. Our study suggests that the version of the MAPT gene that is overrepresented in Parkinson's may cause transportation to slow down in the dopaminergic neurons. This slower transportation may then explain why people with this version of the MAPT gene have a greater chance of developing Parkinson's.

Overall, this study has helped to further our understanding of how common variation in our genomes connects to risk for Parkinson's. By understanding what is happening with the different variants of the *MAPT* gene we know more about the role of the *MAPT* gene and the tau proteins in normal neuron function and disease.



BeEVERS JE, Lai MC, Collins E, Booth HDE, Zambon F, Parkkinen L, Vowles J, Cowley SA, Wade-Martins R, Caffrey TM (2017) MAPT Genetic Variation and Neuronal Maturity Alter Isoform Expression Affecting Axonal Transport in iPSC-Derived Dopamine Neurons. *Stem Cell Reports*. 9(2):587-599. PMID: 28689993.

## Parkinson's UK Oxford Branch News

It has been a busy time for the Oxford branch of Parkinson's UK. The branch has over 250 members and friends and we were pleased to meet many of them at the Oxford Walk for Parkinson's in September. Members have held events including cream teas, a hotdog and pudding lunch, and a pumpkin competition. Branch members have also completed numerous sponsored challenges to raise funds for Parkinson's research including the Royal Parks half marathon, the Vitality London 10k, the BOXCAM bike ride from Bristol to Oxford, and later to Cambridge, and walking the length of Hadrian's Wall. You can read more about these and all the news from the branch at <https://oxfordparkinsons.org.uk/>.

Paul Mayhew Archer has continued to amuse audiences at the Comedy Store and his 25 shows at the Edinburgh Fringe – and very informative and light-hearted it was too. He has attended a lunch hosted by the Archbishop of Canterbury and even managed to get into No 10 for a reception.

In April 2018 Chair Sally Bromley was awarded an Honorary Master of the Open University Degree for Public Service, for her work helping people with Parkinson's and support of medical research into the condition. The branch had previously organised the 2017 Parkinson's 200 plus conference in Oxford marking the bicentenary of publication of An Essay on the Shaking Palsy by James Parkinson. The event was recognised with an "Inform" award at Reading University's Research Engagement and Impact Awards 2018. Talks from the event including contributions from branch members and OPDC scientists can now be viewed via <https://oxfordparkinsons.org.uk/p200plus/timetable>.



### OPDC joins Oxford Walk for Parkinson's 2018

This September, family members joined the OPDC team for Parkinson's UK Oxford Walk for Parkinson's, taking on routes between 1.5 and 8 miles around the city, raising funds and awareness for the condition. Despite an extremely soggy start to the day over 200 Parkinson's supporters joined the walk and OPDC researchers and clinicians had a chance to chat with walkers about research being carried out to improve our understanding of the condition. It was a fantastic day with a brilliant turn-out and we thank the Oxford branch of Parkinson's UK for a wonderful event. We're already looking forward to 2019.



## Pinnochio by Hazel Stanyon



At our 2018 OPDC Parkinson's research day we were joined by Hazel Stanyon, a member of our Discovery cohort. In an excellent talk she shared how she has transformed her life since her diagnosis through exercise to combat Parkinson's, and has set up her own business in furniture design (SuperChic Furniture) specialising in restyling vintage and mid-century furniture. She also gave a reading of her poem, Pinnochio, which she has given us permission to share here.

Don't treat me like Pinnochio  
a wooden doll who has no soul  
I have a heart and feelings too  
but often hidden away from view

Don't treat me like Pinnochio  
whose legs are stiff and do not  
bend.  
They weigh a ton and hamper  
me from being who I want to be

Don't treat me like Pinnochio  
Who cannot speak or say hello  
My voice has got much quieter  
now  
I want to shout but don't know  
how

Don't treat me like Pinnochio  
Who's face is hard with painted  
grin  
I want to smile to show I care  
but all you get is just a stare.

Don't treat me like Pinnochio  
Who has no voice his lips are  
thin  
I want to tell you how I feel,  
I love you so from deep within

My words are all but muffled now  
but inside I am standing tall,  
speaking loud, addressing all  
But on the outside looking in  
all you see is an awkward grin

Don't treat me like Pinnochio  
who has no heart and has no  
soul  
I see your sadness, feel your  
pain and want to hold you once  
again

But as this battle rages on  
I find it hard to still be strong  
I'm sorry that this cannot be for  
Parkinson's has captured me  
I want to laugh and scream and  
shout but when I try it won't  
come out

I see your sense of helplessness  
You wonder what to do  
You feel afraid you want to cry  
You're struggling so much too

You hide your tears away from  
me  
You're trying to be strong  
This beast has got me by the  
throat  
And he drags you along

If I could take this all away  
of course you know I would  
I'd smile at you, I'd run and  
dance  
I'd do all that I should

So when you find the goings  
tough, you can't go on, you've  
had enough  
Please remember me as was  
And don't feel bad because .....

This person who you dearly love  
still remains just battle-scarred.  
The silence, muffled words and  
stare  
can all appear to say - Don't care

Unlike Pinnochio I'm real  
I can feel and I can see  
One day I'm up, one day I'm  
down  
Will today see a smile or today  
see a frown

Tears seem very active too  
I don't know why I don't feel blue  
I suddenly just fall apart  
And show the world my broken  
heart

I know how hard it is for you and  
all that you are going through.  
You give to me and give some  
more  
With my responses being poor

Your care is such a selfless act  
But I am grateful - that's a fact  
To have your love support and  
care  
Enables me to hang in there

The future has no certainty  
We do not know what it will be  
But like the toy we talked about  
We will not scream, we will not  
shout

We'll face the future hand in  
hand  
Pretend we walk on golden sand  
Together we will soldier on  
Facing life - till life is gone.

## In Memoriam: Sheila Cudlip



Sheila worked as a hospital volunteer, meeting and greeting Discovery cohort participants at the John Radcliffe Hospital from 2012 to 2015. Her friendly welcome and offers of tea helped make many participants feel at ease in the research clinic environment. Having developed colorectal cancer, Sheila sadly died suddenly 3 months ago, with her funeral held in the Oxford Crematorium on the 12th September 2018. Half of all donations received at the funeral will go to support future work of the Oxford Discovery cohort. Sheila will be greatly missed by her surviving husband Tony, her son Simon, her daughter-in-law and Cohort PI Dr Michele Hu, and grandchildren Bizza and Ethan.

### Giving to OPDC

At the OPDC we are working hard to understand Parkinson's and to develop new treatments. As we look to the future, we want to ensure that our work is sustainable, and that it can continue for years to come.

If you would like to specifically support our research projects working on Parkinson's at the University of Oxford, you can make a one-off **donation** or set up a regular payment to OPDC via [www.opdc.ox.ac.uk/donate](http://www.opdc.ox.ac.uk/donate).

The OPDC is funded by the Monument Discovery award from Parkinson's UK. If you would like to support the work done nationally by Parkinson's UK, please visit [www.parkinsons.org.uk/donate](http://www.parkinsons.org.uk/donate).

A **Legacy gift** will help the OPDC to continue vital research programmes, to find a cure and to improve the lives of everyone affected by Parkinson's. Large or small, your support will really make a difference to our work.

If you would like to know more about leaving a gift to the OPDC in your will, please contact our administrator Melanie Witt on **01865 282358** or [opdc.administrator@dpag.ox.ac.uk](mailto:opdc.administrator@dpag.ox.ac.uk).

[www.opdc.ox.ac.uk/giving](http://www.opdc.ox.ac.uk/giving)

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