

## Cambridge Branch Newsletter – September-October 2020

Editor  
David Boothroyd 01353 664618  
[d.boothroyd@btinternet.com](mailto:d.boothroyd@btinternet.com)

### BRANCH MEETINGS

**\*\*\*STOP PRESS\*\*\***

**Our Cuppa and Cake Zoom Meeting on Friday, September 25, will have a special visitor taking part: Steve Ford, CEO of Parkinson's UK. He is conducting a series “get involved” sessions with group and branches and we are amongst the first! A great opportunity for your questions, criticisms – and praise!**

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### **CamBioScience's TRAINING COURSES WILL BLEND THE VIRTUAL AND THE PERSONAL**

The July Branch Meeting – of necessity, still a virtual one – featured Michelle Ware, Head of Courses and Conferences at CamBioScience. The company is an innovative organisation established five years ago by leading scientific researchers with the aim of providing customised training courses and conferences, personal and online, in cutting-edge life science technologies.



Members at July's Branch Meeting, with Michelle Ware in the centre of the third row down

Michelle herself has a PhD in developmental biology, and worked in research for 10 years before switching to her current, more training-oriented role. The courses designed and organised by CamBioScience include subjects at the cutting edge of global research, such as the production of 'brain organoids'. These are 'brains in a lab dish', which can be generated from a person's skin cells. They act as neural models, recapitulating the developmental processes and organisation of the developing human brain. They are playing a vital part in activities like

drug screening and brain modelling. In 2019 CamBioScience staged a conference with obvious relevance to Parkinson's on the development of the dopamine system, from stem cells to circuits. Another interesting topic relevant to neurodegenerative conditions, including both Parkinson's and Huntington's, is sleep. But the importance of sleep in repairing the brain is not talked about enough, Michelle said.

Her talk was preceded by a Cuppa & Cake session. We have now had several of these virtual get-togethers, which have proved successful and popular. They could be the norm for quite a time!

### NEWS, EVENTS & PEOPLE

#### **WE NEED A NEW BRANCH SECRETARY!**

Trish Carn, who has been our Branch Secretary for the last few years, has taken on the vital role of Treasurer, so we badly need a new Secretary.

The Branch Secretary gets involved in various tasks. These include: helping to organise the group's activities; creating the agenda for committee meetings, and taking and circulating the minutes of the meetings (held every two months); encouraging other volunteers to get involved; monitoring news coming from Parkinson's UK, and sharing it with members; and ensuring the group runs according to Parkinson's UK governance procedures – ie, follows the rule book!

You will need good administrative, communication and IT skills. PwP can have quite widely differing views and concerns and you will need to reflect these to the group, to ensure the support provided by the Branch is what members actually want. And what is in it for the Secretary? They play a crucial role in the local Parkinson's community, and one benefit you can gain is making new friends and building connections.

If anyone is willing to consider this, Trish will be more than happy to talk about what is involved, how much time is needed, and so on. She will also be available to help the new Secretary, as they get to learn the ropes. So it is not too daunting a task! If you are interested, or know someone who might be, please contact Trish ([trishc.parkinsons-cambridge@gmail.com](mailto:trishc.parkinsons-cambridge@gmail.com)) (07815-541111). She is currently doing both tasks, which is too much for anyone.

### **CHRISTMAS LUNCH CANCELLED**

Sadly, we have been forced to cancel our Christmas Lunch, which was due to take place on Friday, December 11. Two factors have made this unavoidable: the first is the Corona virus, the second the David Rayner Building (DRB).

We had been hoping that the restrictions imposed by the Government on the size of groups that can meet would have been lifted by December, or at least significantly relaxed. Of course, this is not beyond the realms of possibility but it is starting to look increasingly unlikely.

But the other hurdle has made cancellation inevitable – the DRB will not be available by December, as it is being extensively refurbished. And we simply do not have another venue available that is anything like as suitable, in terms of parking, access and facilities.

However instead we will arrange a Christmas Cake and Cuppa virtual meeting with suitable festive entertainments. More details in due course.

On a brighter note, we anticipate that the DRB will become available again early in the New Year and we hope that by then we will be able to stage a lunch for members, which will serve as an extremely appropriate celebration of getting back together again! Details will follow in future newsletters, as and when we have them.

### **A THIRD OF PwP HAVE EXPERIENCED WORSENING SYMPTOMS DURING LOCKDOWN**

A third of people with Parkinson's (PwP) have experienced increased symptoms during lockdown, according to a survey by Lancaster University and Parkinson's UK. The survey asked more than 2,000 PwP and family members, friends and carers about their experience of lockdown. Responses showed that symptoms such as slowness of movement, or

stiffness and fatigue worsened, as did tremor, anxiety or sleep problems. Around 10 percent also reported an increase in hallucinations, which can be caused for various reasons but usually from the side-effects of medication.

Some 34% said reduced access to exercise had had a big impact on their lives. The same proportion had appointments with a Parkinson's Nurse or consultant cancelled, with more than half not offered a phone or online appointment. Of those who received social care and support at home before lockdown, nearly half said they received less care during restrictions.

Although many PwP have an increased risk of severe illness if they get the virus and are in the clinically vulnerable category, they are not classed as extremely vulnerable and therefore not eligible for an increased level of support.

Together with concerns about loneliness and isolation, people reported increased stress because of worries about access to food if there were no neighbours or family to help, and this exacerbated physical symptoms. Another worry is what the 'new normal' will be, and especially the risks for PwP.

Increased caring responsibilities for family, friends and carers also had a negative impact. Some 68% had taken on more caring responsibilities since the coronavirus restrictions started, 42% said the restrictions were negatively affecting their mental health, and 34% their physical health.



Katherine Crawford, Director of Services at Parkinson's UK (pictured), said the results show just how hard the Parkinson's community has been hit by the Corona crisis, both physically and emotionally.

"We know that over a million people with Parkinson's, family members, friends and carers have needed Parkinson's UK more than ever during the pandemic. In response, we have developed our helpline capacity, further supported the online

Parkinson's community and made sure people who normally receive face-to-face support continue to do so in new ways."

### **AmazonSmile DONATES NEARLY £1000**

The latest donation to Parkinson's UK as a result of the AmazonSmile system is worth £978.

AmazonSmile is a simple, automatic way for Amazon users to support the charity of their choice whenever they shop (see [smile.amazon.co.uk](https://smile.amazon.co.uk)).

To date, Amazon has donated a total of more than £5,309 to Parkinson's UK, over £3.6m to all UK charities, and £155m to charities worldwide. Users can track the results of their shopping throughout the year at the AmazonSmile Impact page. AmazonSmile is also available in the Amazon Shopping App on iOS and Android phones.

### **RESEARCHERS EVALUATE CLINICAL TRIALS, WHILE JOURNAL AWARDS ITS FIRST PRIZE**

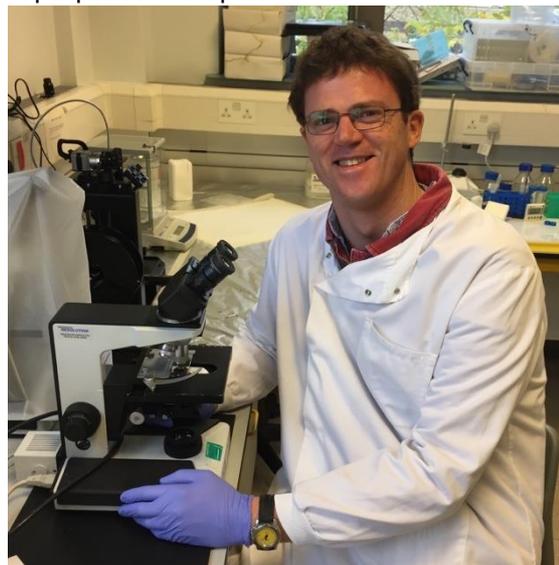
A review of current clinical trials for Parkinson's shows a wide range of both symptomatic and potentially disease-modifying therapies are now being evaluated. Investigators say the outlook for patients is encouraging, given the number of therapies being clinically tested. Their analysis and results are published in the Journal of Parkinson's Disease (JPD).

Most of today's drug treatments were approved for clinical use in the second half of the last century, and they provide only relief of symptoms. In contrast, disease-modifying therapies should slow, stop, or even reverse the condition.

"The discovery of the first genetic risk factors for Parkinson's at the turn of this century is enabling researchers to better understand possible biological pathways that may be influencing the progressive neurodegeneration of Parkinson's," said senior author Simon Stott, Deputy Director of Research at the Cure Parkinson's Trust in London (pictured).

"These discoveries have led to a growing number of clinical trials targeting an increasing number of potentially disease-relevant mechanisms of action. It is important for the research and Parkinson's communities to stay abreast of the extensive, ever-changing landscape in order to highlight trends and better manage expectations."

This is the first broad overview of Parkinson's clinical trials and it reveals the tremendous amount of research being conducted on therapeutic agents, which have many different mechanisms of action and therapeutic targets. Investigators found that there are 145 ongoing clinical trials for therapeutics targeting Parkinson's. Of these, 57 are focusing on long-term, disease-modifying therapies, with 88 concentrating on therapies for short-term, daily symptomatic relief. A total of 50 trials are testing repurposed therapies.



The number of clinical trials under way is encouraging for the Parkinson's community, especially the high proportion of repurposed initiatives that increase the chances of a new therapy becoming available more quickly. The breadth of targets for both symptomatic and disease-modifying therapies shows the value of primary research over many years.

Meanwhile, the JPD has awarded its first ever Parkinson Prize for outstanding contributions to research. The recipients are doctors Thomas Foltynie, Heiko Braak, and Kelly Del Tredici. Two papers were the basis for the prize, which are freely available to everyone to read, download, and share.

The first, by Dr. Foltynie, reported on the exenatide trial, and the second considered brain pathology in Parkinson's. The joint author of the second (with his wife) is Heiko Braak, famous for the theory that Parkinson's may originate in the gut before it travels to the brain.

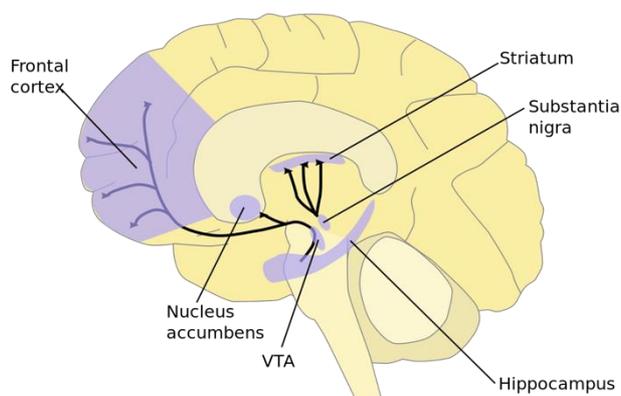
Their papers were selected by JPD from among 461 research articles and 153 review articles published between the journal's launch in 2011 and 2019. The winners will receive a commemorative plaque and a

cash award of \$1,000 per article. The Prize will continue as an annual award, and in 2021 an article published in 2020 will be selected.

## SCIENCE & RESEARCH

### DYSKINESIA MECHANISM EXPLAINED

Many PwP eventually develop debilitating movements called dyskinesia, which are a side effect of dopamine replacement medication. The mechanism underlying this has been unknown, but now US researchers at Scripps Research in Florida have found a key cause, and with it a potential treatment.



Dopamine medication causes an increase of a protein with the unwieldy name Ras-guanine nucleotide-releasing factor 1, or RasGRP1, which ultimately results in dyskinesia. But the team have found that in mice and other animal models, inhibiting production of the protein reduces dyskinesia without negating the beneficial effects of dopamine therapy.

“Parkinson's patients describe treatment-induced dyskinesia as one of the most debilitating features of their illness,” the researchers say. “These studies show that if we can down-regulate RasGRP1 signalling, we can greatly improve their quality of life.”

The team has studied the problem for the past decade, eventually discovering that RasGRP1 was a major culprit. The next step is to find the best way of reducing RasGRP1 in the brain – specifically in the area called the striatum – while not affecting its expression in other parts of the body. However, in mice a total lack of RasGRP1 is not lethal, so blocking it with drugs, or even with gene therapy, may have little or no major side effects.

### IF DBS IS SLOWING DOWN PROGRESSION, IT WILL BE A LANDMARK ACHIEVEMENT

Deep Brain Stimulation (DBS) can both slow down progression and reduce the need to prescribe multiple drugs, compared with medication alone, suggests a new pilot study published in the journal *Neurology*. “We've shown that if DBS is implanted early it's likely to decrease the risk of progression, and if this is borne out in our larger study it would be a landmark achievement in Parkinson's,” said senior author David Charles, of the neurology department at Vanderbilt University in Nashville, USA.

The US Food & Drug Administration (FDA) has approved a 130-patient, multi-site, double-blinded randomised trial of DBS for early stage Parkinson's. If the results of the pilot trial are replicated, DBS will become the first therapy proven to slow down the progression of Parkinson's.



Vanderbilt's Mallory Hacker and David Charles.

As usual, the DBS system used features a pair of ultra-thin electrodes implanted into the brain to deliver electric pulses to the subthalamic nucleus. After five years, the patients who received optimal drug therapy only were five times more likely to have a worsening of their rest tremor, compared with patients who had DBS and drug therapy. The DBS patients also required considerably less medication.

“This pilot study is clearly telling us that the new study must be done to determine whether DBS slows the progress of Parkinson's when implanted in the earliest stages,” Charles said. “This is an incredibly exciting finding, but patients and physicians should not change clinical practice at this time,” he added.

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## VIEWPOINT

### Elizabeth Forbes reflects on this strangest of years

I had always wanted to go to India since my father told stories when I was a child of his experiences there and in Burma during the war. Then it had become a mystical, symbolic place in the minds of many baby boomers and over the years I had absorbed impressions of the religion and culture from its diaspora and from books. It was as though I had saved visiting to be a treat one day. We intended to go when we retired and could find time for our next big trip but as we approached that milestone my husband Martin was diagnosed with Parkinson's. His movement had been impaired for some years with arthritis and as energy and mobility severely reduced it became apparent that it was no longer practicable to go.

Now in this strangest of years I find myself reflecting on these long held aspirations and the acceptance of their surrender. Our nation was plunged into confinement more than five months ago. Those who are retired or vulnerable have been at home, urged to keep out of the way, while younger folk have balanced home-working with home schooling, and key workers have been stretched to the limit. Their efforts have been lauded and applauded, the lives saved celebrated, those lost counted and mourned.

Now we are exhorted gradually to return to a normal life, although directions change week by week. There is much talk of a 'new normal', where face masks and distancing become routine and we try to work out a balance of real and on-line activities in relation to shopping, keep fit, social interactions. It is worth acknowledging how we have changed through this experience: learned how to operate 'Zoom', grasped on-line shopping, perhaps met or chatted more to neighbours, learned a new vocabulary. We have also given the planet some carbon respite, left more space for wildlife. Diverse creatures have moved into spaces we have left unoccupied like National Trust properties and railway stations. The sky has been more blue!

Now as many people are picking up the threads and thinking of holidays, India or any trip seems more distant than ever. This virus has left us in a place beyond where we knew we were, a place with a sense of loss, of isolation, but also where we celebrate a new or rather anew a rhythm of quietness. A local picnic becomes an event. I have learned to identify the meadow brown butterfly as it dips into the garden's nectar, and seen the moorhen chicks grow on Hobson's Brook.

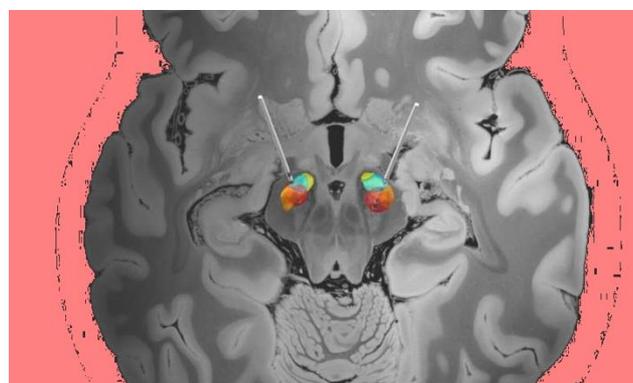
There seems to be a missing thread from here to those in power as I listen to wranglings over China and Russia and Europe and reports of the disease rampant in the Americas. I wish those leaders would stop for a moment too and observe the butterflies.

*(continued from page 4)*

Meanwhile, the Australian QIMR Berghofer Institute in Brisbane has identified ways to make DBS more effective and safer. One potential drawback of DBS is that in some people, it can cause psychiatric problems such as increasing impulsiveness. The researchers wanted to find out if there were subtle differences in the way DBS was affecting their brains compared with other DBS patients who had no such side effects.

They recruited 55 recent patients and used an advanced method of brain imaging, called diffusion MRI, to reconstruct the connections between nerve cells in the brain that were stimulated by the implanted electrodes.

"We used a 'virtual casino', which simulated 'real-world' impulsivity, and looked at how the brain networks influenced by DBS affected gambling," said lead researcher Dr. Philip Mosley. "Participants played the casino before DBS, and again once their stimulator was implanted and turned on, so we could quantify whether the stimulation influenced them to bet in a more risky manner."



They found that when DBS affected the brain's prefrontal cortex, participants were more likely to place bigger, riskier bets after DBS. This region is important for planning behaviour and inhibiting inappropriate actions, so it makes sense that stimulating it can change behaviour in this way. When the clinical progress of all the study participants was followed, it was found that patients who developed clinically significant, harmful changes in behaviour after DBS had a strong connection between the site of stimulation and a specific region of the prefrontal cortex, called the orbitofrontal cortex.

This region has been shown to be important in evaluating a desired goal and assessing a potential

outcome, to work out if behaviour should be modified. Possibly, these individuals developed significant problems because their brains weren't able to perform this function, which meant they didn't link poor choices to negative outcomes, and therefore didn't learn from the experience.

"Our understanding of how behaviour can be linked to the pattern of connections in the brain stimulated by DBS means we can make it safer and more effective," Mosley said. "Knowing which connections are harmful or helpful will assist neurologists and neurosurgeons to decide where best to place the DBS electrodes and how to adjust the device postoperatively so that only regions of the brain responsible for treating the motor symptoms of Parkinson's are stimulated."

### **SIMPLE RULES FOR A GOOD NIGHT'S SLEEP**

Like other neurological conditions, Parkinson's can cause sleep problems, but recent research suggests there are specific things you can do to give yourself the best chance of some decent shut-eye. Here are some "Simple Rules for a Good Night's Sleep", from Jenny Morton, Professor of Neurobiology at Newnham College, Cambridge. They are based on extensive scientific research.

**Computers:** keep outside the bedroom! And don't use backlit screens for pre-bed reading.

**Set a bedtime:** go to bed 30 minutes either side of this time.

**Fix a 'wake-up' time:** this should be 8 hours after your bedtime. Set an alarm and get up when it goes off, even if you still feel tired. (It may take 2 weeks to get used to your 'bedtime' and 'wake-up' times. But stick to them until patterns are consolidated).

**Don't take daytime naps:** if you feel sleepy, do something else – go for a walk, do the dishes, take a shower. If you must take a nap, limit it to 30-40 minutes and set your alarm clock to wake you up.

**Exercise:** take a regular bout of exercise during the day, but don't do strenuous exercise within 2 hours of bedtime.

**Food and drink:** no coffee more than 4 hours after your wake-up time. (For example, if you get up at 7am, don't drink coffee after 11am.)

**No alcohol within 2-3 hours of bedtime**

**Eat a full meal at least 4 hours before bedtime:** you can have a light snack before you go to bed. Foods rich in tryptophan may be helpful: milk, yogurt, eggs, meat, nuts, beans, fish, and cheese. Warm milk and honey, or bananas are possibilities.

**Avoid smoking:** for at least 1-2 hours before bed. If you smoke, cut down. Nicotine speeds up the heart rate, raises blood pressure, and stimulates brain activity.

**Use your bed only for three things:** sleeping, reading and sex! Do not work, watch TV, play computer games. Preferably, don't have a TV or computer in the bedroom. If you must, make sure power is off so there is no light showing.

**Be comfortable:** if you haven't bought a new mattress in the past decade, consider it, also a mattress pad or underlay.



**If you share a bed and both have disrupted sleep:** try using separate sets of sheets and duvets, so you don't compete for them. The temperature should be 18-20°C, the room as dark and quiet as possible. Buy light-proof curtains.

**Mobile telephone must be switched off:** and leave it in another room.

**If you're a natural worrier:** try 'active worrying' – use a worry period during late afternoon or early evening. Write down the things that are worrying you, decide which you can do something about, create a plan of action. Leave the others on the list for another day.

**Don't worry about not sleeping:** humans have an amazing capacity to do without sleep. Contrary to popular belief, insomnia is not lethal. Worrying about not getting to sleep is counter-productive.

**A major function of sleep is resting the body:** just lying quietly in bed reduces heart rate.

**Some people find listening to the radio helps:** radio is much less stimulating than TV.

**If you get up in the night:** don't check email or phone messages.

**Don't adjust your wake-up time** to compensate if you have slept badly. Still get up 8 hours after you went to bed.

## BRAIN REPAIR CENTRE VIDEO DESCRIBES RESEARCHERS' WORK DURING LOCKDOWN

As if to answer the question, "And what did you do during the famous Covid lockdown?" the Brain Repair Centre has produced a video in which several researchers explain their work and how they have managed during this unique period.



One of the Centre's Ph.D. students, Marta Camacho describes her work on gastrointestinal dysfunction in Parkinson's. This can happen up to 20 years before any Parkinson's diagnosis and one key question is whether gut dysfunction can affect the course of the condition. During lockdown, Marta has analysed data which suggests that people with modest to severe dysfunction – in the form of constipation – seemed to progress more quickly and suffer more balance and memory problems than others. She says this could hold important clinical implications. Marta plans to follow this up with a detailed study over three years and is already preparing the questionnaires to collect the data.

The immune system (IS) is the focus of concentration for Nina Kouli, a research assistant in the group run by Caroline Williams-Gray (pictured). There are at least two forms of Parkinson's, a 'benign' version, which progresses relatively slowly and another one where progression is faster and results in memory and other problems. This poses two main questions: do some PwP have a more activated IS, and if so does this contribute to faster progression and memory problems? Nina plans to take blood and spinal fluid samples from volunteers with Parkinson's and also to do PET brain scans, which show the degree of IS activation in the brain. The aim is to assess the subjects after three years to see how they have progressed. Also involved in an IS trial is Julia Greenland, a doctor at the BRC, who is helping Caroline in the trial of azathioprine, a long established drug that suppresses the IS.

Other topics discussed included the Transeuro and Sunrise Parkinson's projects, trialling stem cell implants and gene therapy respectively, described by Research Assistant, Sam Hewitt. Further stem cell work was discussed by the BRC's Research Manager Danielle Daft, and Venkat Pisupati, about the collaboration with the University of Lund in Sweden. Sophie Skidmore described using stem cells to model Parkinson's, with the aim of understanding the mechanism that leads to the formation of Lewy bodies, and potentially make it possible to develop more effective drugs.

Prof Roger Barker then initiated a question and answer session, in which two of the key questions relating to Parkinson's were: the heterogeneity of the condition, namely the degree to which it varies in terms of speed of progression and overall range of symptoms; and the question he gets asked most by PwP: when can I have stem cell treatment?

Does the variability of Parkinson's stem entirely from differences in the response of the immune system? Caroline said there were differences in other genes that probably were involved and we are now reaching the point where we can predict how someone will progress, when they are first diagnosed. This will help in selecting directly relevant treatments for each individual patient.



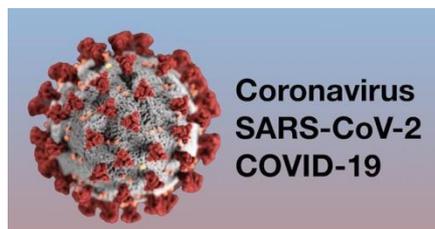
For stem cell therapy, which holds out the prospect of a radical advance in treatment potentially for many PwP, Danielle said the aim is to get a new trial up and running by September 2021. She is now holding meetings with the MHRA (Medicines and Healthcare products Regulatory Agency), which has to give approval for a clinical trial. Ironically, the COVID lockdown has probably helped to move this process forward more quickly than would otherwise have been possible, Danielle said, as it made it possible to concentrate on it fully.

The video lasts just under 54 minutes and is available to view at <https://youtu.be/Qi9O4sDO3ps>.

## JOURNAL ASSESSES EFFECT OF VIRUS ON PwP

A recent article in the Journal of Parkinson's Disease (JPD) discusses concern that PwP are more vulnerable to the COVID-19 virus. For example, Parkinson's can compromise the respiratory system, as shown by the increased risk of pneumonia in patients with advanced Parkinson's. But the potential impact of COVID-19 to PwP extends beyond these direct threats.

Less obvious effects of the pandemic on PwP include the social measures intended to cut risk of infection, demanding drastic changes in lifestyles, requiring a flexible adaptation to new circumstances. This



flexibility is a cognitive operation that depends on normal dopamine functioning,

and many PwP are inflexible because of their lack of dopamine. This lack may also cause a feeling of loss of control and increased stress, which can worsen symptoms and cut the efficacy of medication. However, factors that can protect people from

stress, termed 'resilience', enable individuals to maintain or recover mental health during and after times of adversity. Resilience is associated with traits like optimism, creativity, and intelligence. The current crisis will help to show who copes best with the current situation, compared with those experiencing the greatest difficulties.

Clearly, two further consequences of the pandemic are isolation and reduced physical exercise. A loss of aerobic exercise during the COVID-19 pandemic may exacerbate both motor symptoms and non-motor issues like insomnia or constipation. But a potential positive is the emergence of web-based initiatives, from singing to exercise or dancing classes. The crisis has accelerated their adoption.

Also, COVID-19 provides a unique opportunity for researchers to test how it influences the course of Parkinson's, for example by having large groups of PwP wear sensors, or by studying biological biomarkers. It may enable researchers to assess which factors best protect patients, increasing our knowledge about resilience in Parkinson's.

## CAMBRIDGE BRANCH COMMITTEE MEMBERS

Chair: Charles Nightingale [charlesnightingale4@gmail.com](mailto:charlesnightingale4@gmail.com) 01223-844763 07836-232032

Assistant Chair: Mike Brown [mikebparkinsonscambridge@gmail.com](mailto:mikebparkinsonscambridge@gmail.com)

Secretary: Trish Carn [trishc.parkinsonscambridge@gmail.com](mailto:trishc.parkinsonscambridge@gmail.com) 07815-541111

Treasurer: TBC

Newsletter Editor: David Boothroyd [d.boothroyd@btinternet.com](mailto:d.boothroyd@btinternet.com) 01353-664618 07799-598130

Publicity & Social Media: Annabel Bradford [annabelparkinsonscambridge@gmail.com](mailto:annabelparkinsonscambridge@gmail.com) 07950-685307

Membership: Keith Howlett [keithparkinsonscambridge@gmail.com](mailto:keithparkinsonscambridge@gmail.com) 01954-719601 07885-976194

Myra Moore [mooremyra@hotmail.com](mailto:mooremyra@hotmail.com) 01223-843211 07866-068357

Andrew Stevens [andrewstevens@btinternet.com](mailto:andrewstevens@btinternet.com) 01223-861063 07850-250673

Webmaster, Mike Crofts: 01223-893619, [mikecrofts\('at symbol'\)gmail\('dot'\)com](mailto:mikecrofts('at symbol')gmail('dot')com)

(Replacing @ symbol with ('at') and . with (dot) in the email address reduces the possibility of spam)

Roger Campbell [roger4@virginmedia.com](mailto:roger4@virginmedia.com)

Gabby Farrow (Honorary member): 01223-356433

## USEFUL CONTACTS

Parkinson's Local Adviser – 08088-000303 email [hello@parkinsons.org.uk](mailto:hello@parkinsons.org.uk)

Facebook: [www.facebook.com/parkinsonsukcambridge/](https://www.facebook.com/parkinsonsukcambridge/)

Twitter: <https://twitter.com/CambBranchPUK>

Help Line 0808-800-0303 (free phone call) Specialist advisers can answer questions on any aspect of Parkinson's

Parkinson's Nurses in our area: for help and information contact the Parkinson's Nurse Team on 0330-726-0077

Addenbrooke's Hospital Parkinson's Nurses 01223-349814

Branch Website: <https://www.parkinsonscambridge.org.uk>

Parkinson's UK 020-7931-8080 [enquiries@parkinsons.org.uk](mailto:enquiries@parkinsons.org.uk) [www.parkinsons.org.uk](http://www.parkinsons.org.uk)

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