PARKINSON'S UK CHANGE ATTITUDES. FIND A CURE. JOIN US.

Cambridge Branch Newsletter: January-February 2023

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BRANCH MEETINGS

PACKED HOUSE ENJOYS A CHRISTMAS PARTY FEATURING 'SOMETHIN' ELSE'…

If the attendance by branch members is the yardstick to go by, our Christmas Party is an extremely popular event. There must have been at least 40 to 50 people gathered together in the David Rayner Building on Friday, November 25.

And it was a Christmas party with a difference. As well as the extremely generous raffle, thanks to our friends from John Lewis, we were given a performance from a musical comedy act called Somethin' Else. They are a duo featuring Mike Anderson and Lou Casey.

No one could accuse their act of lacking variety. Starting off with the likes of George Formby, we progressed to Ken Dodd's Happiness, and on to It's a Long Way to Tipperary, Side by Side, and Blowing Bubbles.

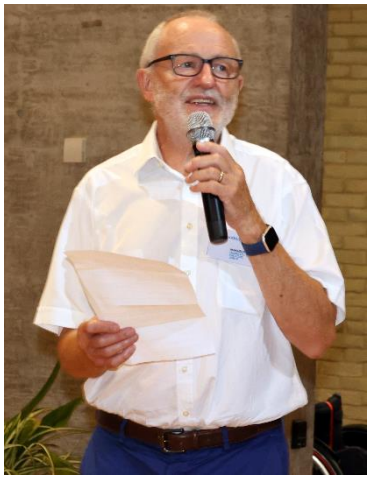
Somethin' Else had no problems at all getting our members to join in with the singing. Indeed, they had several members getting up onto the stage performing with them – without, it has to be said, too much persuasion!

The traditional songs were then followed by a new routine for the duo: an Egyptian-themed act. Naturally, this was only to be expected given that 2022 is the hundredth anniversary of the discovery of Tutankhamen's tomb by the archaeologist, Howard Carter. Of course, we all knew that, didn't we? The show came to an end with a rousing performance of the song "It's later than you think, enjoy yourself." It was obvious that our members had done just that.

A NEW YEAR MESSAGE FROM OUR CHAIR, MARK

Happy New Year to you all!

It was good to see so many of you at our Christmas lunch at the David Rayner Centre – despite the freezing weather. Last year was not easy but we're well on the way to building our branch activities back to strength with the help of our volunteers.



Thanks to our committee for keeping the show on the road during the difficult Covid times. The Cake and Cuppa online meetings have worked really well. I hope they have encouraged those of you who are less able to get to the DRB to still participate in the activities of the group. Keeping and growing that sense of community and mutual support is vital. We currently have a membership of nearly 400, but we are always looking to engage anyone affected by Parkinson's.

Looking back on last year – our 40th – we had a grand celebration with Paul Mayhew-Archer. He is such a pro, both as a performer and in driving publicity for our work. We should try and make more of comedy. It's great therapy. Another plus of the evening was the chance to meet our new Chief Executive, Caroline Rassell. We gave her a branch perspective on the national support for local groups. I'm not convinced that we have yet struck exactly the right balance between local support and national programmes, particularly research. Research is vital but so too is the support we give locally.

Another achievement last year was the setting up of a younger persons group, together with the Peterborough branch. It has started to meet, and is yet to find its stride but it is still early days.

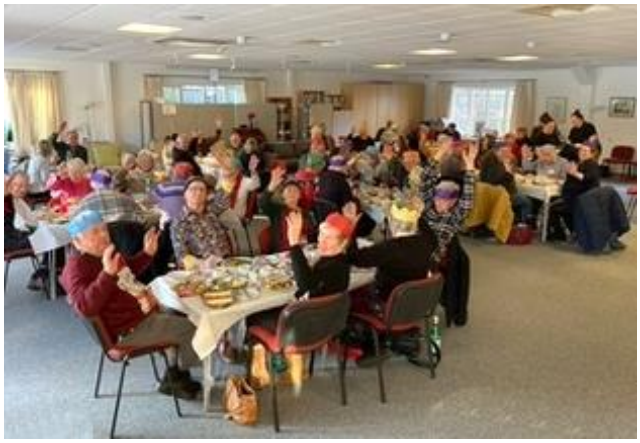
Looking forward, I'm delighted we're setting up a new suite of activities. Personally, I'm championing the yoga with Rebecca. She is excellent and works with folk of differing abilities. I particularly like her because she is not dogmatic – not trying to make us adopt extraordinary poses! She takes us as we are and gently guides us forward. Also, we're hopeful we have found a new volunteer to organise these activities. She is a keen sports person and a great believer in the benefits of exercise.

A big thank you to Annabel for all her great publicity work during the year and welcome to her new baby boy, Jacob.
Keep warm,
Mark

MEMBERS BEAT THE FREEZING WEATHER TO ENJOY THE CHRISTMAS LUNCH

Despite a prolonged spell of some of the coldest temperatures we have had for years, our Christmas lunch went ahead virtually without a hitch.

Almost everyone who had bought tickets managed to get to the David Rayner Building, with the total number being just below 50. Unfortunately, your Editor and his wife were two of the no-shows – but that was the result of a positive Covid test, not the cold!



Our Chairman, Mark, hobbled through his pain (following an operation) and said some words of greeting and thanks to open proceedings.

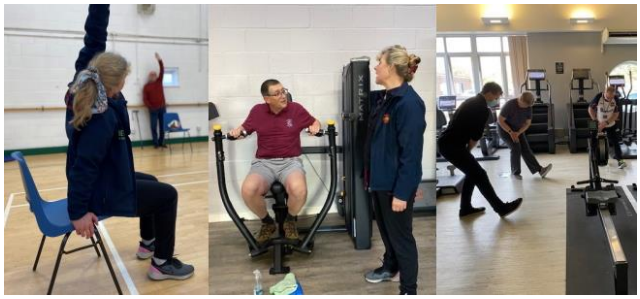
Then it was on with the meal, with white and red wine provided. All in all, a successful lunch in what were quite challenging circumstances. Roll on summer!

NEWS, EVENTS & PEOPLE

COUNCIL'S FITNESS SERVICE FOR PEOPLE WITH LONG-TERM MEDICAL CONDITIONS

Cambridge City Council provides an exercise referral service for people with a long-term medical condition or disability. This prescribes a suitable programme of activity, with each programme lasting 12 weeks or longer and including support, assistance and supervision as required from specialist exercise professionals.

Your tailored programme might include gym-based exercise sessions, exercise classes, or online courses that you can follow from home. There is a cost for the sessions, except for the free home-based events. Assessment by a fitness professional costs £7.50, gym sessions and exercise classes are £3.50 per session.



If you are unsure about whether the service is right for you, speak to your health professional. You can also watch our exercise referral playlist on YouTube, or listen to an episode of the Healthy You podcast about the service. To apply for the referral service, use this link: Apply to join the exercise referral service. If you are a doctor, nurse, occupational therapist, physiotherapist or dietician you can refer a patient to the service. See this link: Refer a patient to the exercise referral service.

"Even if you cannot refer patients, you can support us by providing access to information about the service," says the Council. "We can provide promotional information and videos about the service on request. We can also add you to our mailing list and send you regular updates about the service. Contact us at startup@cambridge.gov.uk, tel 07525-800996."

The main website for the service is: https://www.cambridge.gov.uk/fitness-for-adults-with-long-term-medical-conditions

FIRST CAFÉ GETS GOING AT ARLINGTON AS CAMBRIDGE MANOR PREPARES TO OPEN

Early December saw the launch of our first Parkinson's Café venture, which was hosted by Arlington Manor Care Home. Here, our Membership Secretary, Keith, describes how it went.

"We were inevitably anxious that someone will turn up, and Martin Dickson (Customer Relationship Manager at Arlington), Caroline Bent (our co-secretary) and I sat for a bit and waited, making smalltalk. But we didn't have to wait long.

"We were quickly joined by an Arlington Manor resident and his wife and one other couple who are unable to join our fourth Friday in the month sessions. Both couples are Branch members but have not been to the David Rayner Building," Keith said. "As the conversation developed over tea and coffee, plus some Christmas treats, the four realised they had actually been communicating with each other already, as both are on our WhatsApp group!

"It was a small, intimate and useful conversation that Caroline, Martin and I were delighted to be involved in. Both couples said they found value in the Café and will be back next month on Tuesday, January 3. (Arlington's Cafés are on the first Tuesday of every month).

The first Parkinson's Café to be hosted by the Cambridge Manor Care Home will be on January 19, and from then on, every third Thursday of the month at 2.30pm.

Martin echoed Keith's comments. "Yes, we were extremely happy to start off our new venture with a successful group. As we said, with any new group and venue, it is always a nervous wait but we had a lovely relaxed conversation and were very pleased with how it went. We are looking forward to

building up the numbers gradually over the coming months.

“A big thanks to Keith and Caroline for attending our first event. Also thanks to Julie and Lisa for their assistance to make the idea into a reality.”

SCIENCE & RESEARCH

COVID-19 SHOWN TO TRIGGER SAME BRAIN INFLAMMATION AS PARKINSON'S

Australian researchers at Queensland University have found that COVID-19 activates the same inflammatory response in the brain as Parkinson's. The discovery identified a potential future risk for neurodegenerative conditions in people who've had COVID-19, but could also lead to a possible treatment.

The team studied the effect of COVID on the brain's immune cells – ‘microglia’ – which are the key cells involved in the progression of brain diseases like Parkinson's and Alzheimer's. They grew human microglia in the laboratory and infected the cells with SARS-CoV-2, the virus that causes COVID-19.

As a result, the cells effectively became ‘angry,’ activating the same pathway that Parkinson's can activate, called the inflammasomes. Triggering this inflammasome pathway sparked a sort of ‘fire’ in the brain, which began a chronic and sustained process of killing off neurons.

“It's a silent killer, because you don't see any symptoms for years,” a researcher said. “It may explain why some people who've had COVID-19 are more vulnerable to developing neurological symptoms similar to Parkinson's.”

The researchers found the spike protein of the virus was enough to start the process, which was exacerbated when there were already proteins in the brain linked to Parkinson's. Therefore, if someone is already pre-disposed to Parkinson's, having COVID-19 could be like pouring more fuel on that ‘fire’ in the brain.

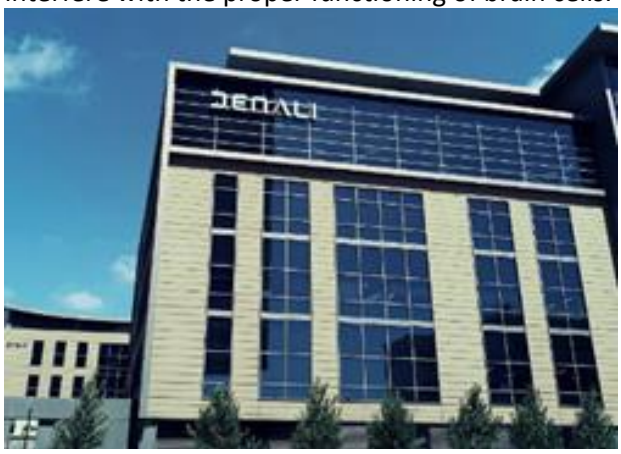
However, the study also found a potential treatment, a class of inhibitory drugs developed at the university, which are currently in clinical trials with Parkinson's patients. These have blocked the inflammatory pathway activated by COVID-19, essentially putting out the fire.

The drug reduced inflammation in both COVID-19-infected mice and the microglia cells from humans, suggesting a possible treatment to prevent neurodegeneration in the future. Further research is needed, but the team say this is potentially a new approach to treating a virus that could otherwise have untold long-term health ramifications.

EXPERIMENTAL PILL IS SAFE, TRIAL FINDS

An oral medication aimed at slowing the advance of Parkinson’s was well tolerated in 150 people who took it over 28 days, according to clinical trial results recently published.

Researchers say their experiments in animals and in cells suggest the treatment can correct failings in the workings of cellular lysosomes. These are cells that remove toxins from the brain. If they are prevented from working properly, toxic proteins build up and interfere with the proper functioning of brain cells.



Denali Therapeutics is a US company based in Silicon Valley that specialises in researching therapies for neurodegenerative conditions. It has developed two drugs, DNL201 and DNL151, which work by preventing the build-up of LRRK2 enzymes.

Previous tests of the experimental drugs raised concerns about potential side effects in humans. Animals given DNL201 displayed high levels of the protein dardarin, which caused the vesicles, small fluid-filled sacs inside cells, in their lungs and kidneys to swell.

VIEWPOINT: DOPAMINE, THE NEUROTRANSMITTER EXTRAORDINAIRE.

Decades ago, dopamine was regarded as just one of many neurotransmitters in the brain, and of relatively minor importance. That changed, almost dramatically, in the 1960s and dopamine is now recognised as one of the most critical substances in the human brain. And as we know only too well, if you haven't got enough, you get Parkinson's.

It is worth summarising briefly the astonishing range of brain functions and effects that dopamine underlies. One of its most famous characteristics is its role as the "chemical of pleasure". (This explains the title of a recent cookery book by TV chef Tom Kerridge, his "Dopamine Diet"). In the medical world, this is regarded as a rather crude popularisation. To describe it more accurately, if slightly more obscurely, dopamine plays a key role in "confirming motivational salience". That is, when we desire something, or feel aversion to it, dopamine is crucial to this happening.

It does plenty of other things: it reduces both insulin production in the pancreas and activity in the immune system; it is central to various neurological conditions apart from Parkinson's, such as schizophrenia, thought to be linked with excess dopamine, restless leg syndrome, attention deficit hyperactivity disorder (ADHD), Tourette's syndrome, bipolar disorder, and addiction.

The activity of various drugs are closely linked with dopamine, such as cocaine, amphetamines and nicotine. These promote increased levels of dopamine, which look to be the primary cause of addiction. Too much pleasure!

Given how crucial a substance dopamine is, and the effects of not having enough, there is something of a mystery attached to it. Each of us is born with what is a relatively small number of brain cells that produce dopamine – 'dopaminergic' neurons. At birth the total is about 400,000, and this falls during a lifetime. Only if it goes below a critical limit do people get Parkinson's.

This figure of 400,000 might sound quite a lot. But put that number into context: the total number of cells in the brain is estimated to be about **85 billion**. So the 400,000 dopamine cells represent around 1/200,000th of the total. And the question that this prompts is: why has evolution equipped us with so few? Is there a reason we don't have far more?. Would it make schizophrenia more likely? Or addiction? This may be a question we never satisfactorily answer. But it is just another intriguing facet of the extraordinary substance that is dopamine.

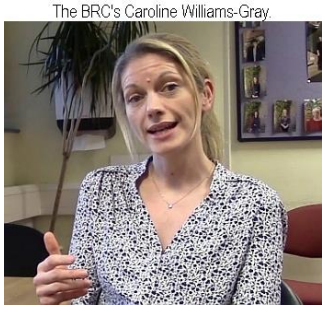
The current study aimed to reduce the effects of dardarin build-up while preserving the therapeutic benefit of restoring lysosome function. The small study, which included mice, rats, macaque monkeys, and humans, did not evaluate the efficacy of DNL201 in slowing down progression of Parkinson's. But it demonstrated that the drug boosted lysosomal function in animal models and did not cause noticeable side effects in humans or monkeys. Because DNL201 must be taken twice daily, Denali has decided to concentrate on its companion drug, DNL151, which only requires a single daily dose.

"It is a very exciting time for Parkinson's research as we have now reached the point of clinically testing novel treatments that have been developed based on a better understanding of the underlying biology," said Simon Stott, Deputy Research Director at Cure Parkinson's.

JPD'S FEATURE FOCUSES ON INFLAMMATION

The latest issue of the Journal of Parkinson's Disease (JPD) has a special feature on the connection between the immune system, brain inflammation and Parkinson's. It discusses the challenges it poses, and considers the development of new treatment strategies targeting the system, aiming to reduce or even reverse neurodegeneration.

The supplement's Guest Editors comprise some of the world's leading researchers into neuro-inflammation, including Caroline Williams-Gray of the University of Cambridge's John Van Geest Centre for Brain Repair' (VGB) located at the Addenbrooke's Hospital site.


The BRC's Caroline Williams-Gray.

A series of studies have provided evidence that the immune system and inflammatory processes are connected with Parkinson's. But the precise cause-and-effect linking neuro-inflammation and the brain cell degeneration that occurs with Parkinson's is difficult to determine. That is because the events that start the whole process probably occur many years before brain cells start to die and clinical symptoms appear.

However, there is growing evidence that inflammation may be in part an actual cause of Parkinson's, rather than being just a consequence or side-effect of the neurodegenerative process.

The risk of getting Parkinson's is influenced by many factors, including a person's immune system, their genetic makeup, and the environment, such as a person's infection history, the researchers say.

The JPD supplement covers a wide range of topics connected with inflammation, including immunogenetic determinants of Parkinson's, the evidence from large population-based studies for there being an immune component involved in the condition, the influence of infections and the gut microbiome, and also between the GBA1 gene mutations and immune changes. The role of specialised cells like T and B lymphocytes, and age-related immune changes are also covered.

"In summary, multiple independent studies in clinical and preclinical models have provided corroborative evidence of the involvement of central and peripheral immune and inflammatory processes in Parkinson's," the Guest Editors say. "Our knowledge of how the immune system contributes to PD pathogenesis is constantly evolving, with increasing evidence for a role of several genes and susceptibility loci." (These are genetic regions implicated in increasing risk of a condition).

A major challenge is to use these research findings to identify specific targets within the immune system, or target toxic proteins involved in driving immune responses. The hope is that this will make it possible to identify subsets of patients who are more likely to respond to immune-changing therapies.

"Clinical trials targeting alpha-synuclein have already commenced and both clinical and experimental trials focusing on different immune components are ongoing," the Editors say.

But they emphasise that research is still needed to pinpoint the individual and collective roles of immune cells, and how they interact both with each other, and with alpha-synuclein and other key proteins.

An important feature of Caroline's work on neuroinflammation is the hypothesis that the immune system could be playing a significant role in causing the widely varying nature of Parkinson's and its progression. In particular, it could be that the activated immune cells in the blood play a critical role by exacerbating the activation of microglia (the brain's immune cells) and causing secondary nerve cell damage.

Her group is investigating this theory by studying immune markers in blood and cerebrospinal fluid, and using PET brain imaging. She is also now leading the first randomised placebo-controlled clinical trial repurposing an established immunosuppressive drug (azathioprine) to see if it can slow down the progression of Parkinson's.

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Facebook: www.facebook.com/parkinsonsukcambridge/
Twitter: https://twitter.com/CambBranchPUK
Help Line 0808-800-0303 (free call) Specialist advisers answer questions on any aspect of Parkinson's
Parkinson's Nurses locally: for help and info contact the Parkinson's Nurse Team on 0330-726-0077
Addenbrooke's Hospital Parkinson's Nurses 01223-349814
Branch Website: https://www.parkinsonscambridge.org
Parkinson's UK 020-7931-8080 enquiries@parkinsons.org.uk www.parkinsons.org.uk

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