P E P NEWS

Newsletter of the Parkinson Education Program of Greater Cleveland

DECEMBER 2015 **Dr. Mark Lewine, Editor**

DECEMBER MEETING

Wednesday, December 2, 2015 – 2:00 p.m. till 4 p.m.

We welcome Dr. David Riley, a renowned neurologist and an annual favorite *PEP* speaker – Dr. Riley will give us his update on Parkinson's disease and the progress made in research during the year.

Cleveland Heights Recreation Center
One Monticello Boulevard, Cleveland Heights, OH

(Last names N through Z, please bring light refreshments)

From David Brandt

- I wonder how many of you got to see the live DBS surgery performed at University Hospitals on the National Geographic Channel a few weeks back. One of the lead doctors was Dr. Benjamin Walters who has spoken at past *PEP* meetings. Not only was the surgery fascinating but it brought to light what a successful DBS operation can do for Parkinson's patients as it so positively showed for that particular patient. It is another example of how far we have come to providing relief and slowing down the progression of the disease.
- We thank Ben Rossi from InMotion for the inspiring talk at our last meeting on the positive effects of exercising for those with Parkinson's and then taking us through several exercises that everyone participated in and enjoyed. It showed how simple exercises can be fun and helpful!
- As you are aware, *PEP* has a Facebook page – Parkinson Education Program of Greater Cleveland. To help in getting more eyeballs to the page, please "like" and "share" the page when you get a moment. Visit the page https://www.facebook.com/Parkinson-Education-Program-of-Greater-Cleveland-538407166282079/?fref=ts to see about what other Parkinson related groups are doing as well as our own group.
- Finally, I hope everyone has a wonderful Thanksgiving. It is a time to think about all of the things in our life that we are thankful for. I hope to see you at our next meeting!

New Artificial Neuron Will Help Restore Neuronal Functions

(Excerpt from www.pcrm.org)

Neurological disorders are currently treated using traditional medications and electric stimulations. A group of scientists at Karolinska Institutet in Sweden has recently developed an organic electronic neuron made of conductive organic polymers. This artificial neuron is able to function like a real human neuron: It can sense changes of chemical signals and translate these signals into an electrical impulse that causes the release of a neurotransmitter (e.g., acetylcholine). The effects induced by the neurotransmitter's release can be further measured on human cells in vitro. This new neuronal model will help to bypass damaged nerve cells and restore neural function, possibly contributing to the treatment of neurological disorders.

PEP January Meeting
January 6, 2016

We will have a day at the movies as we show the recently released film Capturing Grace. It is a film by David Iverson that features a legendary dance company and people with Parkinson's joining forces to create a performance of a lifetime. Popcorn and drinks will be provided to enhance our day at the movies!

Robin Williams had dementia with Lewy Bodies – So, what is it and why has it been Eclipsed by Alzheimer's?

(Excerpt from TheConversation.com – November 6, 2015)

Depression, paranoia, Parkinson's disease, confusion and dementia. The long list of symptoms suffered by Robin Williams is itself confusing, but all of these and more besides, can be accounted for by the disorder bearing the name, dementia with Lewy bodies (DLB), which his widow has now announced as his final diagnosis.

Few people have heard of DLB until, like Williams' family, they are confronted by its multiple and variable combinations of symptoms which fluctuate in severity in an alarmingly unpredictable manner.

Yet DLB is the second most common cause of dementia in older people, accounting for 10-15% of all dementia cases and affecting at least 100,000 people in the UK alone. Only Alzheimer's disease itself is more common.

Despite this, as the founder of the Consortium on Dementia with Lewy Bodies which has, over two decades, developed global consensus on guidelines for the clinical and Robin Williams' recent death put the condition in the spotlight. Ver en vivo En Directo/flickr, CC BY-SA pathological diagnosis and management of this common disorder, I am aware how littleknown it is.

A STRANGE AND SHOCKING ILLNESS

Lewy bodies were first described in the early 20th century by Dr Friedrich Lewy, who was studying the brains of people with Parkinson's disease, a condition recognised by a combination of a shaking tremor, slowness of limb movements, and a shuffling walk.

Lewy bodies are, in fact, microscopic clumps of a protein called alpha-synuclein which may, under certain and as yet not understood circumstances, accumulate within nerve cells in the brain. When some critical brainstem and midbrain structures including the substantia nigra are involved, there is a loss of the neurotransmitter dopamine and Parkinson's disease is the result.

But in the last 20 years or so, we have realised that Lewy body disease can also affect other parts of the brain, producing symptoms other than those of Parkinson's. It occurs in the autonomic and peripheral nervous system producing vegetative symptoms such as low blood pressure, constipation and sweating.

DEFINING SYMPTOMS

Lewy bodies occurring in the cerebral cortex, meanwhile, lead to the characteristic symptoms by which DLB is recognised, usually starting with mild and fluctuating disturbances in attention and wakefulness.

The affected person appears vague, drowsy or frankly confused with a decrease in their interest and ability to reason or to carry out practical tasks. Apathy is one term used for this and is frequently mistaken for depression.

Visuo-perceptual function is also affected early which may account for the report of Williams' bruising "miscalculation with a door", and it is this involvement of the visual system which underpins the occurrence of the lifelike visual hallucinations which occur in about 80% of cases and often alert the clinician to a DLB diagnosis.

WAKING NIGHTMARES

Hallucinations may be threatening or distressing but are often simply perplexing for patients who cannot understand why familiar faces or unknown intruders repeatedly appear to them. For others, the hallucinations occur as nightmares as part of a specific sleep disorder. As the Lewy body pathology disease progresses, generalised cognitive impairment and dementia progressively worsen, although a fluctuating pattern with intervals of lucidity often persists.

Parkinsonism occurs in many but by no means all sufferers and in those like Robin Williams in whom it seems to have been quite early and prominent, the initial diagnosis given is often one of Parkinson's disease, a dementia label following soon after as additional symptoms emerge. Short-term memory failure, the hallmark of Alzheimer's disease may not be prominent unless, and here's where it starts to get complicated, there is also a lot of Alzheimer's disease pathology in the brain as well.

HARD TO PIN DOWN

Why did it take so long to recognise the existence of DLB, especially if it is so common? The answer, is that cortical Lewy bodies are vanishingly difficult to see in the brain using conventional staining methods, unlike their brainstem counterparts observed so long ago by Dr Lewy.

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Robin Williams had dementia with Lewy Bodies – So, what is it and why has it been Eclipsed by Alzheimer's?

(cont'd from page 2)

Nevertheless, the development of immuocytochemical staining methods in the early 1990s suddenly made them visible outside of specialised units. This was a major step forward.

But what progress is the research community making with DLB now? Internationally agreed criteria for the clinical and pathological diagnosis have been agreed since a meeting held in Newcastle upon Tyne in 1995, updated there in 2005 and due to be reviewed and updated again in December this year.

Dedicated research centres such as the NIHR-funded Biomedical Research Unit in Lewy Body Dementia at Newcastle University have led the field by, for example, developing diagnostic tests such as the dopamine transporter SPECT scan, which can distinguish DLB from Alzheimer's with >85% accuracy and which is now widely clinically available.

NEW HOPE

Therapeutic trials have been few and far between in DLB because of a combination of a lack of compounds to test, a pre-occupation with targeting Alzheimer's and a reluctance of regulatory bodies to recognise DLB. All of these are now changing and DLB is increasingly viewed as a malleable and commercially-viable target.

Pharmacological trials in DLB will undoubtedly increase public awareness and for families such as Robin Williams' there are now highly-effective patient and carer organisations that provide information, advice, advocacy and support research activity.

As an inter-form of Parkinson's and Alzheimer's disease, DLB has the potential to unlock the key to both of its related disorders. It is high time it was put in the spotlight.

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Rapamycin Prevents Parkinson's in Mouse Model of Incurable Neurodegenerative Disease

(Excerpt from www.thebuck.org, September 2015)

Rapamycin, an FDA-approved drug that extends lifespan in several species, prevented Parkinson's disease in middle-age mice that were genetically fated to develop the incurable neurodegenerative motor disease that affects as many as one million Americans. While the rapamycin did great things for the mice, scientists in the Andersen lab at the Buck Institute also got an unexpected plus from the research – a new understanding of the role parkin plays in cellular dynamics, one that challenges the current dogma in Parkinson's disease research and presents new opportunities for drug discovery. The study is currently online in the *Journal of Neuroscience*.

"Given its side effects as an immunosuppressant, there are issues with long-term use of rapamycin, but the results of our study suggest that use of derivatives of rapamycin or other agents with similar biological properties may constitute novel therapeutics for the disorder," said senior scientist and Buck faculty Julie Andersen, PhD. "Our discoveries regarding parkin may provide an even more important therapeutic target for Parkinson's disease."

Parkin is a protein encoded by the PARK2 gene in humans. Mutations in PARK2 are most commonly linked to both sporadic and familial forms of Parkinson's disease; they diminish the cell's ability to recycle its internal garbage. Parkinson's disease is characterized by the accumulation of damaged proteins and mitochondria in the area of the brain where the neurotransmitter dopamine is produced.

Rapamycin prevented Parkinson's disease symptoms from occurring in middle-aged mice who had a human mutation in the PARK2 gene. Researchers in the Andersen lab expected this benefit to come via the accepted role of parkin – they thought rapamycin would boost the mutated protein's ability to label certain types of cellular garbage for recycling. Instead they discovered that parkin plays a much broader role in the actual recycling of garbage and the manufacturing of new mitochondria.

"This is a completely new, unrecognized, function for parkin," said Andersen. "Our work shows that parkin plays a much broader role than was originally thought in getting rid of damaged mitochondria and proteins. It's

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***PEP* NEWS**
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FIRST CLASS MAIL

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(cont'd from pg. 3)

very exciting because it gives us new ways to look at potential therapeutics to boost cellular clean up."

Working in both neuronal stem cell models and mouse tissue, scientists found that rapamycin not only boosted the mutated protein's ability to label cellular garbage, but also affected the process of recycling the garbage itself via up-regulation of a protein known as TFEB which increased the degradation and purging of both damaged proteins and mitochondria via a process known as lysosomal autophagy. Apart from rapamycin's effects, Andersen's team also discovered that parkin is involved in mitochondrial biogenesis – via up-regulation of PGC1alpha, a protein which drives increased mitochondrial synthesis.

Problems with autophagy, which result in the accumulation of damaged proteins and organelles, have long been linked to Parkinson's disease," said Ana Maria Cuervo, MD, PhD, professor and recipient of the Robert and Renée Belfer Chair for the Study of Neurodegenerative Diseases at Albert Einstein College of Medicine in New York City. "This novel role of parkin in the regulation of the overall process of autophagy gives us new ways to address its dysfunction in Parkinson's disease."

"Researchers are already very interested in parkin as it relates to Parkinson's disease," said Andersen. "I'm hoping that uncovering this novel role for the protein will bring it center stage as an extremely important therapeutic target for the disorder."

TRIBUTES

We need your donations to continue bringing you the *PEP* News and for other expenses. A special thanks to those who contribute at the monthly meetings. To send a donation, please make your checks payable to Parkinson Education Program and mail to – 17930 Birch Hill Drive; Chagrin Falls, OH 44023

TRIBUTE

Alan and Sally Tatar