

East Midlands

RSN NEWS

from the East Midlands Research Support Network

*** July 2014 / No 18 ***

Welcome to the 18th edition of East Midlands RSN News. We start this edition by offering congratulations to our Chairman, John Telford, on becoming a member of the national RSN Development Team. With his extensive knowledge and practical, common sense approach to things, together with his energy and commitment, the Development Team can only benefit hugely from his membership. Also, RSN members in the East Midlands have someone who could be a channel for their views and comments. We are pleased to include John's update on the Development of the RSN in this issue.



(Neuron, by renjith krishnan: freedigitalphotos.net)

We also have a very informative article from John in which he suggests possible directions for research into Parkinson's and other neurological diseases in general.

A group of 7 recently visited Nottingham University to view everything involved in the MR Imaging and Tracking Parkinson's project and we have a report on this visit from Roger Elkin.

The closing date for registration to our 3rd Annual Research Forum is fast approaching and the number of

Inside this issue:

- **Steering Group** 2
- **News & Events:**
 - RSN Steering Groups ... 2
 - PaMIR visit 4
- **Did you know?**
 - Triple Focus 6
- **Coming up** 8
- **Next issues** 9

... and much more!



(Support Computer Key, by Stuart Miles: freedigitalphotos.net)

Parkinson's UK is the operating name of the Parkinson's Disease Society of the United Kingdom. A charity registered in England and Wales (258197) and in Scotland (SCO37554)

delegates already registered to attend is steadily growing. The subject is “Research into Exercise for Parkinson’s: Finding out what really works” and a number of eminent researchers will be passing on their knowledge. It is known that exercise is beneficial and the information at this Forum will be of great benefit to people with Parkinson’s. So don’t miss out on getting hold of this information and register without delay. More information and registration details are on [page 10](#).

Finally, this is the last issue which I will be editing, the role going back into the very capable hands of Caroline Maxwell. So I would just like to thank everyone who has contributed to East Midlands RSN News during the last year or so, making my role a lot easier, and I wish Caroline all the best for the future.

Ian Billcliff, Editor

We were sad to learn of the tragic death of **Vina Shah**, Branch and Volunteer Support Officer for East Midlands Parkinson's UK. Vina has been associated with the Leicester Branch for over fifteen years and provided support and guidance to volunteers and committee members throughout the East Midlands. We send our sincere condolences to all the family.

STEERING GROUP

CHAIR:

John Telford, Leicester
jntelford@ntlworld.com

SECRETARY:

Lionel Paulo, Leicester
ljpaulostk@talktalk.net

MEMBERS:

Richard Brown, Sleaford,
Lincolnshire

Roger and Kath Elkin, Preston
Capes, Northants

Chris Johnson, Derby

Caroline Maxwell, Daventry,
Northants

Maria Rice, Nottingham

Graham Thorp, Shepshed, Leics

Harry Wade, Parkinson’s UK
East Midlands

News & Events

The RSN – achieving objectives

In the last edition of EMRSN News I wrote about the national meeting in Birmingham in May, which was about developing the RSN. Since then the Parkinson's UK Research Team and a couple of members of the RSN Development Team have thought about what concrete action should now be taken to make the RSN more effective and to expand it throughout the country.

Steering Groups

They have proposed that three task groups (called Steering Groups) of volunteers and staff be set up to work actively towards three important objectives. These are:

- greater participation of volunteers as subjects in clinical trials
- greater involvement of people living with Parkinson's in the



(Network, connecting people, by cuteimage; freedigitalphotos.net)

Increasing awareness and understanding

The proposals about the third steering group do not go into any detail yet about what might be done to pursue the objective of 'increasing awareness and understanding of research'. Indeed what does this statement mean? Of the possible meanings, we in the East Midlands would include:

- speaker meetings
- regular contact with researchers
- explanatory articles in the newsletter

There is a lot of support and even enthusiasm for such things. But what we hope that the RSN Development Team might especially champion is the pooling of newsletter articles that are not region-specific. You will be aware that we include a lot of articles



*(Laboratory equipment, by Photokanok;
freedigitalphotos.net)*

that try to explain research and the science behind Parkinson's and many people outside the region receive RSN News because they find this kind of material interesting and valuable.

A good number of speaker meetings and lab visits regularly take place in other parts of the country and East Midlands members would surely be interested in the topics covered by these. So we think there is a case for working together nationally to produce a flow of articles and reports that all could access. Sharing the work could be very effective.

What Next?

The RSN Development Team will have met again by the end of July and should have set in train the process of recruiting for the Steering Groups. Look out for announcements so that you can apply. Being part of a Steering Group will be worthwhile but also enjoyable especially as you will find yourself amongst friendly and like-minded people.

And, of course, you are always welcome to join us in the East Midlands RSN Steering Group – just contact me or Lionel (see [page 2](#)). All offers to help out in smaller or bigger ways are always most welcome. And working with our regional group is also both enjoyable and rewarding!

John Telford

Have you seen the latest edition of "Progress"?

Just go to <http://www.parkinsons.org.uk/content/progress-magazine>

And why not visit the PUK Research Forum at the same time - <http://www.parkinsons.org.uk/forum/research> - and perhaps join in the discussion.

Visit to the Parkinson's Magnetic Resonance Imaging Repository (PaMIR) programme, 12th June 2014

A small but enthusiastic group of seven representatives from the East Midlands Research Support Network travelled to the Queen's Medical Centre where Dorothee Auer and team members Stefan Schwarz, Graham Collins and Lily Xing presented an update of the research at the University of Nottingham being undertaken as a subset of the Parkinson's Magnetic Resonance Imaging Repository (PaMIR) programme.

PaMIR is part of the Parkinson's UK funded Tracking Parkinson's study, with regular updates presented to East Midlands RSN Researchers' meetings over the last two years - see reports in EM RSN News editions 4, 7, 10 and 16.

Dorothee first reminded us of the Nottingham team's mission which is to:

- develop and evaluate diagnostic and prognostic biomarkers of Parkinson's
- facilitate/promote implementation of validated biomarkers in clinical trials and practice
- become an international leading centre in Parkinson's imaging research.

A biomarker, or biological marker, generally refers to a measurable indicator of biological state or condition.

Topics in the presentations covered an update to PaMIR including the 'swallow tail' imaging marker, progress on neuromelanin imaging, exploration of Transcranial Ultrasound Sensitivity (TCUS) to diagnose Parkinson's and a new way to study brain network changes, all of which is supported by use of the **eXtensible Neuro Archiving Toolkit (XNAT)**.

Graham provided an overview of the XNAT, which facilitates management, productivity, and quality assurance for the PaMIR Imaging Repository data. Newly processed data which includes neuro-imaging MRI scans is captured and securely imported into XNAT from which various categories of user may be granted controlled access for their own specific purposes.



(Medical ultrasound diagnostic machine, by cooldesign, freedigitalphotos.net)

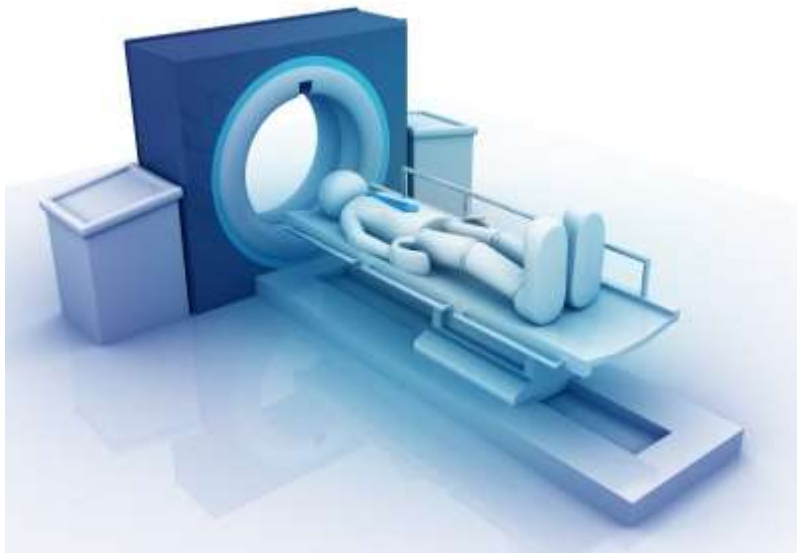
Stefan summarised the current status of PaMIR confirming that ethics approval is now in place and the project is commencing collection of MR imaging data of 400 subjects (300PD and 100 non PD controls) co-recruited in due course from the Tracking Parkinson's study. Half will participate in follow-up rescans in 18-months' time. The team's success (94%) at identifying Parkinson's sufferers by the loss of the distinctive 'swallow tail' image at the back of the substantia nigra will be further

developed to refine the technique and assess sensitivity and reliability. This has the potential to provide quicker and more accurate diagnosis within many UK hospitals where lower powered 3 Tesla (3T) scanners are generally available. A more detailed report of the 'swallow tail' appeared in EMRSN News edition 16 (May 2014) under the heading "Imaging and Tracking Parkinson's" (go to https://www.parkinsons.org.uk/sites/default/files/emrsn_newslettermay2014.pdf)

The visitors asked whether image data from a recent MRI cranial scan that someone may have undergone for some other reason, could be used for PaMIR purposes. The reply explained that scanner settings are specific to the PaMIR parameters so unfortunately this would not be possible.

Advances in MRI testing can better measure neuromelanin, the dark pigment found in the substantia nigra neurons that are gradually lost in Parkinson's. Earlier findings indicated this loss of neuromelanin to be stage-dependent in Parkinson's Disease. The new study, building on previous findings, will determine if this reduction in neuromelanin correlates accurately with dopaminergic neuron loss, potentially leading to development of a new biomarker of disease progression.

A further study to determine if Transcranial Ultrasound (TCUS) can be used to assist in the diagnosis of Parkinson's is also being developed to determine if the readings provide sufficiently sensitive information compared to MRI. Whilst TCUS can be used in a clinical situation and does not use radiation, it is dependent on the availability of ultrasound equipment together with a suitably trained operator. However appropriate expertise is not well established in the UK and up to 10% of people have an insufficient 'bone window' in their cranium to allow this procedure.



(3d MRI Scanner, by cooldesign; freedigitalphotos.net)

Lily concluded the presentations by describing the study on brain network changes. The objective is to identify which areas of the brain link to each other functionally to help understand which network alterations relate to symptoms of Parkinson's and perhaps help in diagnosis. How network changes relate to brain stem cell loss and may be modified by treatment will also be investigated. Participants need to lie still in a scanner for 5-8 minutes to attain a resting state by emptying their minds whilst not falling asleep! Ultimately these research projects aim to develop highly reliable, sensitive brain imaging techniques delivering accurate diagnostic and progression markers for Parkinson's Disease.

After the presentation we enjoyed a tour of The University of Nottingham Radiological Sciences unit, where a visit to the ultrasound section allowed Stefan and Lily to demonstrate some of the TCUS techniques previously described.

This was followed by a viewing of one of the MRI scanners, after ensuring that all visitors were free of pacemakers, aneurism clips, medical pins, incompatible artificial joints or medication pumps not to mention keys, watches and credit cards, so that the strong magnetic field did not interfere with our wherewithal or wellbeing.

At the conclusion of the tour we each thanked our Nottingham hosts for taking the time to provide a well organised and most informative afternoon.

Roger Elkin

Did you know ...?

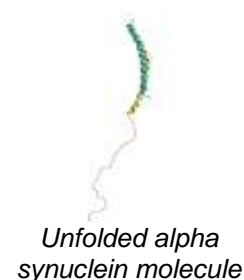
Triple Focus

Templating, Transmission and Types give Triple focus for Treatment discovery

A cell may be small but it is packed full of thousands of different types of molecule and minute structures. They all have their different roles to play and when things go wrong there can be wide-ranging consequences.

There is one protein in nerve cells which seems to be central to Parkinson's. It is called alpha-synuclein and you are likely to have heard it mentioned before. It was so named because it was first found in the **synapses** and **nuclei** of nerve cells. The normal function of alpha-synuclein is not yet fully understood.* But in patients with Parkinson's and other neurological diseases it is found that molecules of this protein have stuck together to form what are often described as 'clumps'. This sounds a bit like a ball of string getting tangled up but the process is really far more structured than this. I am making this point because over only the last couple of years some important subtleties have been discovered about this aggregation process which not only explain how diseases like Parkinson's progress but also give focus to attempts to slow or stop their progression.

Alpha-synuclein is not the biggest of proteins** but nevertheless has a lot of molecular sub-units of different types strung together to form a long chain. Usually this chain is not folded up so it flops about like a piece of string, as it were. But random motion can cause it to fold up in a number of ways – and then unfold again. Certain parts of the chain have an affinity for other parts on other molecules of the protein and so molecules can begin to get together 'like spoons inside a drawer' with certain folded configurations being preferred to enable this.



The point is that, under certain conditions, alpha-synuclein molecules, each with the same folded configuration, can form small groups, called oligomers, and stay that way. Too much of the protein in one place, local inflammation or a small mutation or chemical change in the protein itself are examples of the conditions that can cause this.

'Templating'

But now there is increasing evidence that oligomers of alpha-synuclein with molecules folded in certain configurations can actually induce other molecules to fold in the same way and to stack together. This has been referred to as 'templating' where one small group of folded molecules acts as a template for other molecules to fold in the same way and 'clip' onto the group and so on as a chain reaction. It is rather like how a crystal grows.



Small amyloid fibrils formed from 'stacks' of protein molecules

I wrote about this in [RSN News 11](#) (Dec 2013). Another recent example of research which supports this idea was published in March this year reporting that extracts taken post-mortem from brains of people with Parkinson's caused the aggregation of native alpha-synuclein in the brains of mice into which they were injected. (Ref 1) So Parkinson's is increasingly being seen as a prion-like disease akin to mad cow disease and CJD. (Look up 'Prion' in Wikipedia for an explanation if you need one).

Transmission

Likening Parkinson's to prion disease seems particularly appropriate as other research is indicating that this 'templating' or 'seeding' process can progress from nerve cell to nerve cell over long distances. So it is conceivable that it can start in the gut (as has been long suspected) and move along nerves up to the brain where the connected and especially vulnerable centres (like the substantia nigra which contains the dopamine-producing cells) are affected. Work by Patrick Brundin over recent years has been exploring this (Ref 2).

Types or 'Strains' of templates

But there has been another recent significant finding in addition to the 'templating' and transmission ones. This is that there appears to be more than one way in which the alpha-synuclein molecule can harmfully fold up and aggregate. What's more, different folding configurations of the same protein, alpha-synuclein, could be linked to different neurological diseases. For instance work published last year (Ref 3) showed that brain material from patients who had had Multiple System Atrophy (MSA) produced a similar, MSA-type, degeneration of brain cells in mice into which it was injected. Presumably this was due to a particular folding configuration or 'strain' of alpha-synuclein that is specific for MSA.

Triple focus

All this, to me, suggests a promising new triple focus for research into neurological diseases:

1. Look for ways of stopping the 'templating' of other protein molecules by harmfully folded ones,
2. Look for ways of preventing the transmission from cell to cell
3. Pool research resources between neurological diseases – because it increasingly seems that they share a common pathology.

The above is a simplification of the recent research results and their implications but I think that these discoveries represent an enormously significant step forward.

* One role may be in helping to regulate the release of dopamine:
http://en.wikipedia.org/wiki/Alpha_synuclein

** The molecule of alpha-synuclein is actually 140 amino acid units long. It strikes me that this is also the maximum number of characters you can put in a 'Tweet' on Twitter. So maybe this article should be called **Toxic Tweets!** The 'templating' referred to above is a bit like re-tweeting. The press is full of reports of instances where malicious tweets have been re-tweeted over and over again and all sorts of harm has been caused. Once a chain of toxic re-tweeting is started it is very hard to stop.

References:

1. Recasens et al., "Lewy body extracts from Parkinson disease brains trigger α -synuclein pathology and neurodegeneration in mice and monkeys." *Ann Neurol*. 2014 Mar;75(3):351-62 <http://www.ncbi.nlm.nih.gov/pubmed/24243558#>
2. Rey, Brundin et al, "Transfer of human α -synuclein from the olfactory bulb to interconnected brain regions in mice", *Acta Neuropathol* (2013) 126:555–573, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3789892/>
3. Watts et al, "Transmission of multiple system atrophy prions to transgenic mice", *Proc Natl Acad Sci U S A*. Nov 26, 2013; 110(48): 19555–19560, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3845125/>

Images are from Wikipedia and Wikimedia.

John Telford

Coming Up ...

Tues 30 September - Thu 2 October 2014:

World Parkinson Coalition Scientific Update

- free webcasts on vital research topics. Registration ought to be before end of July. For programme go to: <http://www.worldpdcoalition.org/?page=2014WebcastProgram>

Sat 11 October 2014, 10.00 – 15.30h:

East Midlands RSN 3rd Annual Research Forum

The Regent Suite, Park Inn, Mansfield Road, Nottingham NG5 2BT - The theme is "**Research into Exercise for Parkinson's: Finding out what really works**". Further information and registration details are below on [p 10](#).



(Forum smartphone, by Stuart Miles; freedigitalphotos.net)

Sun 2 November 2014:

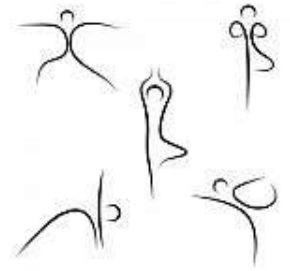
3rd National Research Supporters Day

Royal York Hotel, Station Parade, York
Bookings may be made from August by e-mailing researchevents@parkinsons.org.uk or phoning 0207 963 9356

Full information on events throughout the country can be found on the Parkinson's UK website, by visiting <http://www.parkinsons.org.uk/researchevents>

East Midlands Research Support Network (RSN)
3rd Annual Research Forum:

Research into
Exercise for Parkinson's:
Finding out what really works



Saturday 11 October 2014, 10.30 – 15.30h
at Park Inn, 296 Mansfield Road, Nottingham NG5 2BT

Introductory overview:

- **Dr Nin Bajaj, Nottingham University**

Progress towards a cure and better treatments for Parkinson's

Three expert presentations exploring the research evidence about exercise and Parkinson's:

- **Dr Lucy Annett, University of Hertfordshire:**

Exploring exercise to protect the brain

evidence from animal models that exercise may protect against nerve cell death

The benefits of dance for Parkinson's symptoms

international evidence for improvement in motor and psychological symptoms

- **Dr Sue Lord, University of Newcastle:**

Brain and Body – Getting the most out of exercise

a mind and body approach to getting the best out of different types of exercise including using video gaming consoles

- **Chris Onslow, Training Academy Managing Director:**

Practical evidence from exercise training for Parkinson's

Also:

Panel of Experts to discuss effective techniques and the merits of different forms of exercise



To register for this **free** event please send an email to office@em-rsn.info by **Monday 15 September 2014** with the following information for each participant:

Title: First Name(s): Surname:

Telephone Number: E-mail:

Also state any special dietary or other requirements.

Alternatively phone in the information to Lionel Paulo, 0116 282 7340,
or send it by post to: Lionel Paulo, RSN 2014 Forum, 2 Vyner Close, Leics, LE3 3EJ

Next Issues...

Due to holidays, there will be no EMRSN News in August.

Just a few of the topics to be covered in the next few issues:

News & Events

Further updates on the Development of the RSN and national research priorities
Report on the October Forum

Has this been Researched?

Relationship between jobs and risk of developing PD
Pain and PD

And much more

[Return to top](#)

EMRSN News is published monthly by the Steering Group of the East Midlands Research Support Network (RSN). The RSN brings together people driven to help find a cure and better treatments for Parkinson's. Through our network, anyone can get involved in research and raise funds and awareness for Parkinson's research.

The views expressed EMRSN News are not necessarily those of the Editor, the Editorial Group, the EMRSN Steering Group or Parkinson's UK.

Please send us your questions, contributions and a copy of your newsletter and event notices.

Editors: Ian Billcliff & Caroline Maxwell
(caroline@paddockend.com or 01327 310901)

Editorial Group: Lionel Paulo, John Telford, Harry Wade, Chris Johnson

We look forward to hearing from you!

Visit our page on the Parkinson's UK website:

<http://www.parkinsons.org.uk/content/east-midlands-research-support-network>

There is also a new section on the Parkinson's UK forum dedicated to the RSN:

<http://www.parkinsons.org.uk/forum>