



Brain Bank newsletter

A vital gift



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Imperial College
London

 Parkinson's
Disease Society

New international research into hallucinations and Parkinson's, thanks to the Brain Bank



Dr Susan Fox is a UK-trained movement disorder neurologist. She is working at the University of Toronto, Canada, in collaboration with Dr Antonio Strafella and Dr Jonathan Brotchie, at the Toronto Western Research Institute. The team is studying what causes some people with Parkinson's to experience

hallucinations and develop psychosis, with the aim of improving prevention and treatment.

What causes some people with Parkinson's to have hallucinations?

Many people with Parkinson's are affected by disturbing visual hallucinations which can seem extremely real. Some people feel as though they are being chased or watched, and become paranoid as a result. Others can experience vivid nightmares.

It's unclear why some people with Parkinson's suffer from hallucinations while others do not. They could be caused simply by changes in the brain, or by a combination of both the condition and the effects of anti-Parkinson's medications, such as dopamine agonists and levodopa.

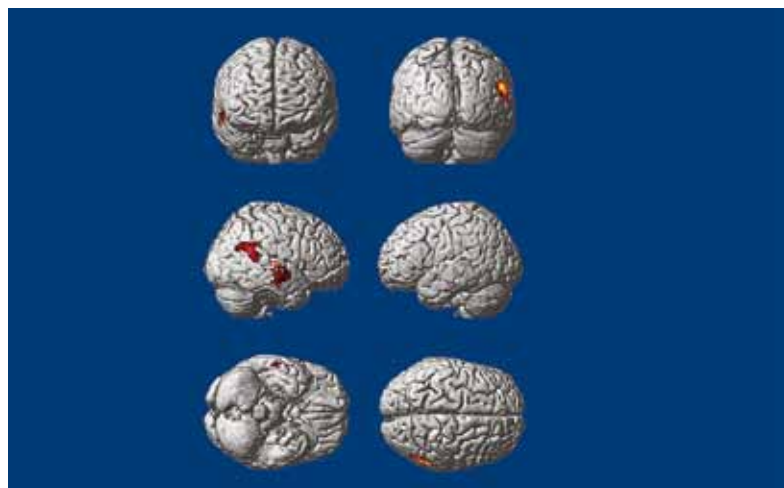
The chemical messenger serotonin is involved in changes in mood, and may play a part in causing visual hallucinations. Other researchers have also found pathological changes in certain brain regions in people with Parkinson's who experience visual hallucinations, indicating that specific brain regions may be affected.

What the team is looking for?

Using brain tissue supplied by the Brain Bank, the researchers are measuring changes in different types of serotonin receptors (which bind with substances such as neurotransmitters), in those regions of the brain thought to be affected in people with Parkinson's with visual hallucinations. Comparing these changes with tissues from people with

Parkinson's who didn't hallucinate, and with healthy brains, should provide clues about why hallucinations happen, and targets for new treatments.

These results will help shed light on those from another study which is investigating changes in certain types of serotonin receptors in people with Parkinson's with, and without, visual hallucinations. (This study is funded by the Parkinson Society Canada.) Early results in six people with Parkinson's suggest that there may be changes in a brain area, the medial temporal lobe, which processes complex visual information in people with visual hallucinations (shown in red in the picture below).



(B Ballanger, AP Strafella, M Zurowski, GS Smith, P Rusjan, T van Eimeren, A Wilson, S Houle, S Fox (2008) *Mov Disord*; 23 (suppl 1);218)

What's been found so far?

Early results have shown that there are changes in some serotonin receptors' activities in the medial temporal lobe in people with Parkinson's who have experienced visual hallucinations. The next step is to investigate which other brain areas are also involved.

How will this research benefit people with Parkinson's?

If studies confirm these findings, then designing drugs that target specific serotonin receptor families could be useful in treating the distressing symptoms of psychosis and visual hallucinations in Parkinson's.

Case study: Joan Grycuk



Joan Grycuk and her son Michael (second from the right) and family

Joan Grycuk, who had Parkinson's, donated her brain to the Brain Bank in October 2005. Joan's son, Michael, spoke to Kirstin Goldring, Parkinson's Brain Bank Manager, about her decision.

“My mother always made it clear that when she died, if medical people wanted to use parts of her body for research then she was happy for this to happen. She had decided she wanted to donate parts of her body to help others.”

Mrs Grycuk was 81 when she died, and Michael described her as being very fit up to that point, apart from the problems with Parkinson's.

“She was a very independent and resourceful woman. She walked everywhere and had travelled the world. She never asked for help from anyone, so developing Parkinson's was very difficult for her.”

The family was initially unsure of whether to go ahead with tissue donation when Joan died, but Michael felt it was important to fulfil his mother's wishes.

“On the day she died, I said to the family that mum had wanted to donate tissue. The family was not sure whether to bother, as she had said it some time ago. I told them that is the point: you say it so people know, and can do something about it when the time comes, as you may not be able to tell them again.”

Michael didn't immediately know what to do to in order to fulfil his mother's request.

“At the time, we looked up the Parkinson's Disease Society's website and saw the information about the Brain Bank and that it was asking for donations. The Brain Bank website was well laid out and it was a very easy procedure to follow, and everything was done very efficiently,” he explained.

The process of the actual donation was described by Michael as very quick with little fuss or trouble.

“Seeing her afterwards did not distress the family at all. They were hardly aware anything had happened,” he said.

Michael also spoke of the importance of people becoming donors, like his mother.

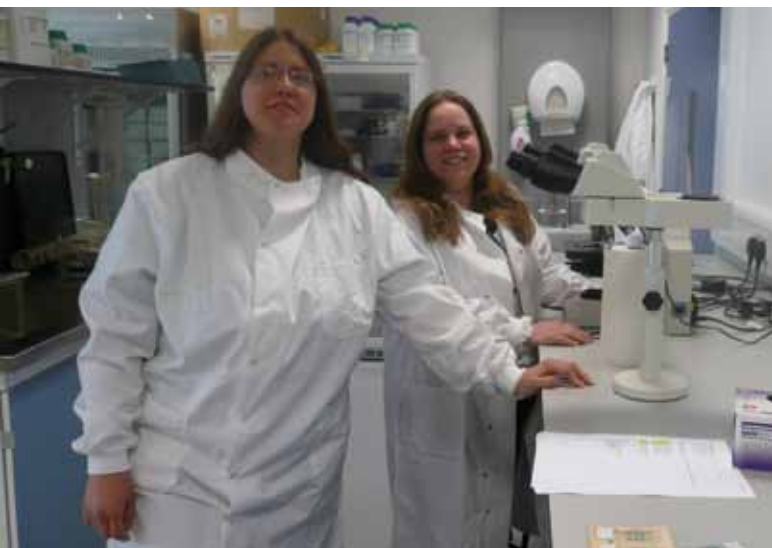
“If you don't do research into diseases or illnesses, then you will never find a cure, and progress stops. Often it's the relatives who become distressed at the idea of their loved one becoming a tissue donor, but it was my mother's expressed wish to help someone else, and I didn't hesitate to do so.”

If you would like to share your story and reasons for registering with the Brain Bank, or tell us why your loved one decided to do so, please email pdbank@imperial.ac.uk, or call 020 7594 9732.

Louise McGuinness, Brain Bank Technician

Louisa McGuinness has been a research technician at the Brain Bank for almost six years. Here she describes the important role she plays in helping find a cure for Parkinson's.

What I do can be divided into working with fresh and fixed tissue (which has been preserved in a chemical fixative), and dealing with tissue requests. The vast majority of my time is spent on dealing with fixed tissue. This tends to set the schedule for my typical working week.



Louise (left) with colleague Regina

First we collect the tissue

This can happen at any time and, as we have to move quickly to ensure that the brain tissue is in the best possible condition, it takes priority over everything else. During work hours, Regina and I take collection in turns. While one of us is in transit, the other prepares the laboratory for the dissection. Out of hours, these tasks fall to members of the on-call team. As we have registered donors throughout the whole country, we could travel anywhere. The furthest I have been to collect tissue is the west coast of Wales, setting off from home about 7am, picking up the tissue early afternoon, and arriving at work about 9pm. That was a rather long day!

Generally, the dissection takes an hour and a half and requires a team of three – a co-ordinator and

two assistants. During the dissection, one half of the brain is cut into small blocks and frozen, and the other is placed in fixative so that it can be used to look for changes in the brain due to disease.



Cutting the brain into blocks

The next step

Once the fresh tissue goes into the freezer, it generally remains there until requested for research. For the fixed tissue, however, the work is just beginning. As we continually collect tissue, there is a constant turnover of cases.

Fixed dissections happen on Tuesday mornings. Depending on how many brains are ready to process, we may dissect two in the same session. The neuropathologist cuts the brain into slices, examining it for visible signs of disease and taking samples for further analysis. The rest is cut into blocks and frozen in a similar manner to the fresh tissue. The dissection and the freezing procedures each tend to take about one hour per case.

Before any of the stored frozen tissue can be given out to researchers, it has to be characterised. It's important to know exactly what type of disease is present in the tissue and how extensive it is. Researchers usually have very specific requests in this regard, and the donor's next of kin often find this information about their relative helpful too. ►

Characterisation

This stage involves the samples that the neuropathologist took for analysis during the dissection. I embed the tissue blocks in wax and cut very thin sections, which I collect onto microscope slides ready for staining which helps us look at structures in tissues. We use a standard panel of stains to characterise each case. Dye-based techniques give an overview of the tissue anatomy and show up any obvious abnormalities, or features associated with Parkinson's disease and other disorders.

Over to the neuropathologist

Once a case is complete, I go through it with the neuropathologist so he can make a preliminary diagnosis and request any additional stains that may prove necessary. We try to schedule case reviews like this once a week, and may screen multiple cases at once. Once I've done the extra stains (if there are any), then my part in the process is finished. The neuropathologist will examine the stained slides in detail and write up his findings. The Brain Bank clinician then writes up an assessment of the donor's symptoms, based on the information in their medical notes. The neuropathological and clinical assessments form the case report, which includes a diagnosis. The case information is vital for ensuring that we meet researchers' requirements when supplying tissue.

Helping researchers with tissue requests

Researchers may request fresh-frozen, fixed-frozen or paraffin-embedded tissue. This may be in the form of blocks, or cut sections on slides. Dr Goldring (Parkinson's Brain Bank Manager) identifies suitable cases and regions, and passes the details onto either myself or Regina. Fulfilling tissue requests is time-critical and has to fit in to the workload to ensure deadlines are met.

The research carried out using the tissue is vital

It isn't easy telling people what I do for a living. It seems to either start conversations or stop them dead! I'm often asked why do I do this job. Well, there are two main reasons: it's challenging and it's important.

It's challenging because I continue to learn, both about Parkinson's and about laboratory techniques. I use that knowledge to continue developing the techniques we use.

It's important because without the technicians, the Brain Bank wouldn't be able to supply tissue for research into understanding the causes of Parkinson's and, ultimately, developing a cure. Knowing that I play a role in that is what makes it all worthwhile.

Meet the team

Dr Kirstin Goldring, Manager, tells us about the day-to-day running of the Brain Bank



Dr Goldring, Laura McKay, Dr Dexter and Regina Vontell

Apart from myself, the team consists of our secretary, Laura McKay, and two laboratory technicians, Louisa McGuinness and Regina Vontell.

I joined six years ago and have been involved from the start in setting up and developing the Brain Bank. I promote what we do to different audiences, and act as an essential liaison point for everyone. I also manage all the day-to-day office and laboratory activities.

I spend a lot of time talking to prospective donors and their families, our funder – the Parkinson's Disease Society, healthcare professionals and researchers wanting to use donated brain tissue. We need to ensure that the Brain Bank is up to date with tissue processing, and the way we store information and keep accurate records. It's also vital that we follow the ethical and Government guidelines for tissue donation, storage and distribution. ►

Our secretary, Laura, is often the first point of contact with potential donors and their families. Laura is responsible for sending out information on donors to research institutions, as well as arranging the collection and distribution of tissue, organising travel for Brain Bank staff and co-ordinating the Brain Bank and Management Board meetings.

Dr David Dexter is Scientific Director, and he oversees all aspects of the day-to-day running of the Brain Bank, including financial and scientific aspects. Along with myself, Dr Dexter is also actively involved in publicising the work of the Brain Bank to prospective donors, healthcare professionals and the research community. Dr Dexter also presents his research studies and the work of the Brain Bank at Parkinson's research meetings in the UK and internationally, where he receives feedback on the types of tissue required.

Dr Ronald Pearce is the Clinical Director. He reviews the clinical notes from all donors to the Brain Bank, and collates the information to produce clinical summaries to accompany the neuropathological analysis. Dr Pearce was instrumental in the development of the lifestyle and medical history questionnaires that we send out to potential donors. Dr Federico Roncaroli and Dr Stephen Gentleman

provide detailed neuropathological reports on all the cases coming in to the Brain Bank, and advise on processing of tissue.

You can find more about the roles of our technicians by reading Louisa's article on page 4.

Providing 24-hour support

We couldn't do what we do without our on-call rota staff. It's crucial to have people on call 24 hours a day, 365 days a year, ready to respond to the death of a registered donor, and to be able to arrange speedy collection and processing of their brain tissue. This requires a co-ordinator and two assistants on call at all times, ready for action. Our on-call support is provided by the Brain Bank staff, the Scientific and Clinical Directors, and postdoctoral and postgraduate researchers from the department. Together, we provide a pool of five co-ordinators and between eight and 14 assistants to fill the rota outside normal working hours.

On behalf of the Brain Bank and the Parkinson's Disease Society, we would like again to thank all of those who have donated tissue, for your contribution to Parkinson's research.



A vital gift

Help us cure Parkinson's

The Parkinson's Brain Bank collects brain tissue generously donated by people with and without Parkinson's. We provide this tissue to researchers around the world who are working hard to find:

- **what causes Parkinson's**
- **a cure and better treatments**

Help us continue this essential research and drive towards a cure for Parkinson's. Register with us today and donate your brain as a vital gift when you die.

Call 020 7594 9732

Email pdbank@imperial.ac.uk

Visit www.parkinsons.org.uk/brainbank

Write PDS Tissue Bank at Imperial College
Division of Neuroscience and Mental Health
Burlington Danes Building
Imperial College London
160 Du Cane Road
London W12 0NN



Parkinson's
Disease Society

Change of address

Name: Donor number:

Old address:

New address:

Front cover photo by James Clarke, *The Times*