

# BIPOLAR

# TWIN STUDY

**First off:** from all of us, a big thank you for your participation in the study, you've all been great to work with. We really appreciate your giving up your time to help. Truly, without your help, none of our work would be possible.

**Aims of the Study:** Just to remind us all why we are doing this work! As many of you will know, either personally or through your twins, living with bipolar disorder (manic depression) can make life extremely difficult, placing many obstacles in the way of living a 'normal' life, as many would wish to. It is essential that we increase our understanding of this disorder if we wish to improve our ability to help those who suffer from it.

**So what are we looking for?** Various differences have been reported between those who suffer from bipolar disorder and those who do not, and these differences appear to exist even when patients are feeling well. Such differences have been reported in Event Related Potentials (Mei Hall), in brain structure and activation (Dr

Sridevi Kalidindi and Fergus Kane) and in performance in tests of cognitive function (Dr Eugenia Kravariti and Fergus Kane). In our study we are looking to confirm whether these differences exist. If they do, we will then try to work out whether they can be explained by a person's genetic makeup or external factors such as stressful life events and obstetric complications.

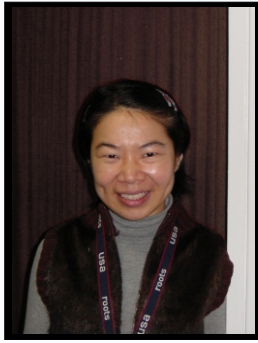
**Twin studies are ideal** for disentangling the influence of genes and environment on brain function and behavior. Identical twins share 100% of their genetic makeup, while non-identical twins share only 50%. Therefore, if a characteristic is more similar within identical twin pairs than within non-identical twin pairs, we can infer a genetic influence on it. If not, external factors, such as stressful life events or disease-related parameters (e.g. medication), are more likely to play a role.

**Knowing the main causes** of these differences is very important. If they are environmental or disease-related, we may take practical steps to reduce the impact of the causes involved. Knowing which abnormalities are genetically determined, on the other hand, can help genetic studies narrow down their search for predisposing genes. In the future, it may be possible to look at a patient's genetic and cognitive profiles and work out which drugs and which forms of therapy may be most beneficial to them.



From left: Dr Sridevi Kalidindi, Dr Eugenia Kravariti, Fergus Kane

## Event Related Potentials (ERPs)



Dr Mei Hall

An Event-Related Potential (ERP) is a change in brain electrophysiological activity in response to a stimulus (such as a tone), and is obtained by averaging a large number of electroencephalogram (EEG) recordings. The ERP recordings are represented as a pattern of waveforms which can be measured in terms of latency (occurrence in time), amplitude (size) and scalp distribution. ERP provides a non-invasive, sensitive and stable quantitative measure of brain function.

### ERP Components of particular interest:

#### P300

The P300 ERP waveform reflects switching attention to a specific target. Its amplitude is believed to index working memory update of changes in the environment whereas its latency is related to speed of brain processing.

#### Mismatch Negativity (MMN)

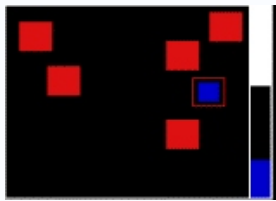
MMN is believed to reflect a change detector mechanism in our sensory memory, an important mechanism for detecting changes in the environment and subsequently reacting to such changes.

#### P50

P50 waveform provides a measure of an information-filtering mechanism in the brain. Filtering out irrelevant information makes brain processing more efficient and helps to avoid the brain becoming overloaded by unimportant information.

We are particularly interested in three ERP components as each of them measures a different brain function. These waveforms have been found to be associated with bipolar disorder. Clarification of the genetic liability between bipolar disorder and ERP components is critical for discovering chemical pathways in the brain and lead onto the identification of susceptible genes.

## Neuropsychological Assessments



Neuropsychological tasks examine cognitive processes, such as attention, learning, abstract thinking and the ability to solve problems.

Thank you to all the twin pairs (45 so far!) who have successfully completed the neuropsychological protocol of the study. Initial analyses of our expanding dataset indicate that twins with bipolar disorder have intact general cognitive ability, and that subtle deficits in specific processes, e.g. the ability to recall the items of a word list, might be due to mild depressive symptoms that persist in periods of relative remission. Another

interesting finding was that twins with bipolar disorder and their unaffected co-twins adopted a rather conservative approach to one of our tasks (involving pressing a pad every time a target sequence of three letters, e.g. '3 5 7', appears on the screen), giving as many correct detections, but significantly fewer false alarms, than twin pairs with no bipolar disorder! It will be interesting to see if these findings will still hold when we have collected enough data.



## Magnetic Resonance Imaging (MRI)

As part of the study, we conduct structural and functional MRI scans with as many of our subjects as possible.

**Structural scans** provide us with detailed images of the structure of grey and white matter within the brain. This will enable us to investigate whether there are any differences in size between the different structures and regions of those with bipolar disorder and those without.

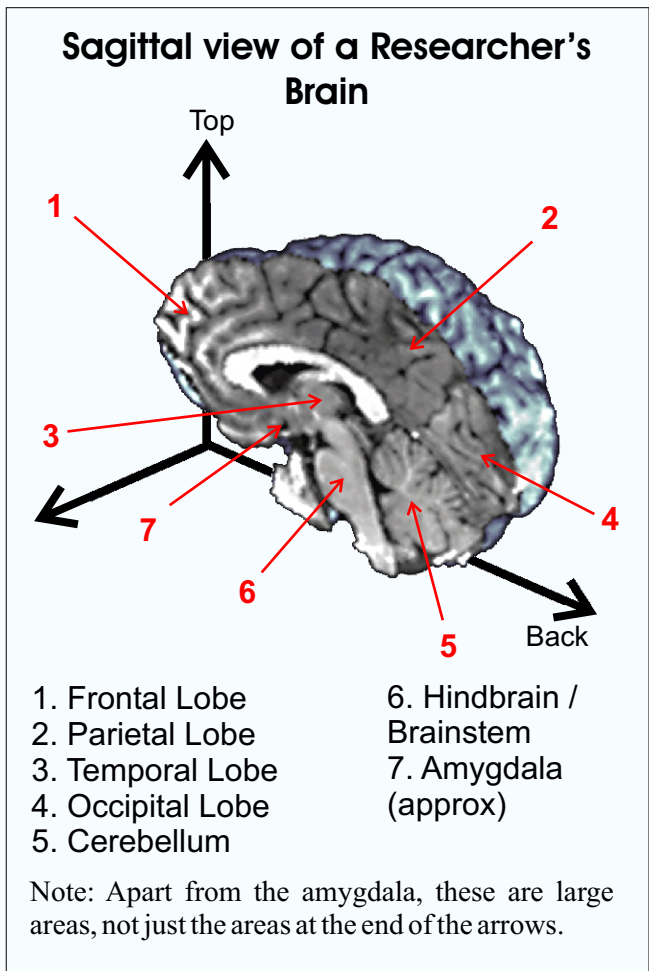
**Functional Scans** are different; the images

acquired are less detailed structurally. Rather, these images indicate which regions of the brain are most active. We often ask subjects to carry out tasks whilst we conduct the functional scans. We can therefore use functional MRI (fMRI) to investigate whether there are any differences in the level and areas of activation between those with bipolar disorder and those without. For instance, Dr Kaladindi has found that during certain tasks involving the processing of emotions, people with bipolar

disorder may show unusual activation of the amygdala (an area known to be intimately involved in emotion). more than those without bipolar disorder.

### Your MRI Scans

Those of you who have completed the magnetic resonance imaging (MRI) scan should find a picture of their brain enclosed. We normally use one of three cross-sections when looking at the brain: sagittal (sliced from the front to the back of the head in a vertical slice), coronal (sliced from left to right in a vertical slice) and horizontal (sliced from top to bottom). The images you have been sent are a sagittal midsection and are the same as the slice of my brain in image on the right. The only difference is that your images are not in three dimensions and they also show the skull and jaw as well as the brain. There are many guides to brain anatomy on the internet. For example, try this one: <http://www.pbs.org/wnet/brain/3d/>



### Living with Bipolar Disorder - Peter's Story

**Below is a short extract from a chapter written by one of our volunteers ('Peter' is his *nom de plum*). We hope that it will provide some insight as to what life can be like with bipolar disorder.**

My illness is triggered by stress in one form or another. I'm 53 now and I've been living with these problems for 21 years. I don't work and I realise that I'm never likely to get a job now. I've tried applying for jobs just on the basis of my CV but it shows that I've changed direction three times without apparent reason. There are also large gaps in my employment when I've been in hospital or unable to work because of my illness. One period was ten years long and when you have those sorts of unexplained gaps, employers smell a rat. [...].

I started my working life as a nuclear physicist, I've got a PhD in physics, what used to be called high energy nuclear physics but is now called elementary particle physics. Then I got a job in low energy nuclear physics which is nuclear fission and reactors and had to adapt my skills to do that but I managed to keep the job for eleven years. I was living near Poole in Dorset because of my job and there I met my wife. I was 32 and not long married when I ended up in hospital with my first breakdown. However after I'd had my second breakdown I promised my company that if I had a third I would resign.

I found I still wasn't able to cope with some unresolvable marital problems and firmly believe that my first two breakdowns were a direct

consequence of these problems. [...].

True to our agreement my company sent a letter reminding me of my promise, so I had no other option but to give them my notice. And not only did I leave hospital without a job but my marriage had to come to an end as well. [...].

I lived a very isolated life and ended up in hospital in Hartlepool which wasn't far from where I was working at the time. I was in a male only ward and I became paranoid. I wasn't sure who I might have talked to about my intimate problems - if anyone - and what their reactions might have been. I won't go into details about what I could have said, but all the time I was anticipating getting knocked on the head by one of the big blokes on the ward and I was very nervous.

But as soon as I moved into a hospital in Durham, with mixed sex wards, helped by my cousin who lives there, I got on better with people and my paranoia went. It was there that for the first time I was diagnosed as manic depressive. Until that point I believed that I suffered from something called nervous debility because it was the sort of thing they used to put on my sick notes. [...]. I was prescribed lithium to balance my moods and I'm still on it, though it doesn't work totally because I've been in hospital maybe four times since then. [...].

A month after leaving I got on a course to do an MA in computer sciences up in Sheffield. [...].

After I got my MA I again started applying for jobs. I applied for over 200 and went for several interviews but out of them only got offered two jobs. One was at Brunel University but unfortunately I was just about to go into hospital again so I had to turn it down because I didn't know how long I was going to be away. [...].

While I was there a nurse caught me with a screwdriver in a power socket. I was checking behind it to see if there was a fourth wire which would indicate that the room was bugged. At that time I was pretty paranoid though I didn't recognise it in myself. Anyway, after I discovered there was no fourth wire I screwed the socket back on which was when the nurse caught me. I was never in any danger of getting an electric shock. I was paranoid, not stupid. But it gave the doctor an excuse to send me to a secure hospital in

Leicester where the wards were locked all the time. [...].

I am a regular attender at the Labour Party and I do their minutes. I am also secretary of the local Tenants and Residents Association so my computer comes in handy to do work for these groups. I'm also on the executive committee of MIND, although I haven't been involved recently. The problem is that their minutes often clash with those of the Labour Party so I may have to give up my MIND work. I'll be sorry to do it, but the point is that when you suffer from nervous problems, it's much easier to make friends with people in the same position. But working with the Labour Party I'm mixing with normal people and they accept me as such this is very important to me. They put me up for jobs and I'm a very active campaigner. Of course, all these jobs are purely voluntary I don't get paid for any of them but the important thing is to keep busy. I'm determined to lead as fulfilled and useful life for as long as I can.

### **More Tests!!!!?**

We are considering extending the project to incorporate some more tests. If you wish to take part, a member of our team will visit you at a convenient time and ask you to perform simple tasks for no more than 20-25 minutes. We will be in touch to let you know about these, and, of course, we do not expect you to take part if you don't wish to.

### **Notices**

#### **WE STILL NEED MORE TWINS:**

Please, if you know of any other twins that may be interested, let them know about the study.

#### **Discordant Twin pair wanted for possible BBC documentary.**

We have been contacted by a researcher from the BBC who is considering making a documentary about a twin pair when one twin has a disorder such as bipolar or schizophrenia. If you are interested in taking part, please contact us and we will put you in touch.

#### **Would you like to talk to other twins in the study?**

Some of our volunteers have suggested that it would be good to speak to other twins who have taken part in the study, particularly those who have bipolar disorder. This would enable you to share your experiences with each other. It would be possible to put together a list of twins who would like to contact each other. If you are interested in this idea, please get in touch.

#### **Ideas for the next newsletter:**

To make the next newsletter interesting, we would like to include some contributions from twins who have taken part, especially contributions that are related to bipolar disorder. Anything will be considered, from poetry to paintings to personal accounts.

#### **Lost in the post???**

It is possible that reimbursement cheques for expenses could get lost in the post and we would not know. If you are expecting cheques and have not received them, please let us know and we will investigate the matter promptly.

#### **Please, stay in touch!**

It is important that we know of any changes in your contact details, so that we can keep you informed of our findings and any future developments in the twin study. We would appreciate it if you could kindly contact us and let us know of any changes in your name, address, phone-numbers or email.

#### **Contact Details:**

Dr E Kravariti (Jenny): 02078480331, e.kravariti@iop.kcl.ac.uk  
Fergus Kane: 0207848003, f.kane@iop.kcl.ac.uk

#### **Online Information:**

We will try to keep updated information about the study on our website:  
[Http://www.iop.kcl.ac.uk/iopweb/departments/home/default.aspx?locator=557](http://www.iop.kcl.ac.uk/iopweb/departments/home/default.aspx?locator=557)  
(Also we should soon have a better link)

**Finally..** Thank you once more for taking part. It's been a pleasure working with you all.