Plans for 2019

Research can be frustrating and it is certainly time consuming. It is also collaborative and exciting. In this newsletter we have tried to give you a flavour of some of what is going on. You will see that our first vagus (vagal) nerve stimulation study using the externally worn ‘Nemos’ stimulator has come to an end and the findings have been submitted for publication. This is a very important step as having research published means that the work is reviewed by independent experts and is made public. Hopefully the findings stimulate others to repeat the work and to take it forward and in doing so new treatments eventually become available.

One big advantage with vagus nerve stimulation (VNS) is that it is already approved by the regulatory authorities in the UK for the treatment of epilepsy and therefore any side effects or risks associated with the treatment are already known. VNS using an implanted device, as in our first study, has been used extensively and found to be very safe. This remains an active area of research for our group as although it takes some time for VNS to start working, the findings suggest that it is very effective. In addition, these observations with VNS have helped us better understand why people with PWS are prone to such outbursts.

Lucie Aman has been working very hard on the mental health study selecting and developing the assessments and getting everything to work. This has turned out to be more challenging than originally thought but we are now there and many of you will be hearing from her shortly. In the pilot study we are looking for adults with PWS to help but in the main study we hope to include children aged 12 and above as well as adults. Lucie will keep you all informed of any updates.

Suzannah Lester’s study is with infants and young children with PWS. We want to better understand at what age a pre-occupation with food is first apparent. The general teaching is that this happens in early childhood but we believe it may be present much earlier. If this turns out to be the case this may impact on early social development. Suzannah will be in contact with parents who have children in the necessary age range. For more details see the article later in this newsletter and do contact Suzannah directly with any questions.

The study Jennifer Noh is undertaking is rather different. We were very much aware during our earlier VNS studies that we were using rather primitive ways of collecting data (paper and pencil!) and that we were losing out on information that might be valuable. Jennifer is working with the App developer, Monsenso, to try and develop a wearable device such as a watch, that can be used to record behaviour but also will collect data on heart rate, sleep, and physical activity. If this is successful this will enable us to better understand how treatments such as VNS are working. Jennifer may ask a number of people with PWS to wear a smart watch and to use the App.

Finally, I would like to mention the research of Elena Bochukova – not covered in this newsletter. She is a basic scientist who used to work in a major obesity research group here in Cambridge but she now has her own laboratory at Queen Mary’s College, University of London. She is seeking to unravel how the genetics of PWS leads to problems in the brain which then lead to over-eating etc. She has recently published a very important paper based on her research examining tissue from the hypothalamus obtained from four people with PWS at post mortem. She is extending this research using the advanced stem cell techniques whereby skin tissue can be converted into stem cells and then into brain cells in the laboratory so that they can then be studied.

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This work has only been possible because of the generosity of Jo and Rob Gambi (they have a son Sam with PWS) who some time ago funded the collection of the cells and the work needed to convert them to brain cells. This initial work was done by Dr Rick Livesey and colleagues at the Gurdon Institute in Cambridge (Gurdon was awarded the Nobel Prize for his work on stem cells). Elena is also working in collaboration with Madeline Lancaster at the Laboratory for Molecular Biology in Cambridge to apply the most advanced techniques to study these cells. In the long run we must answer some of these fundamental questions as to what are the links between genes, the brain and behaviour. So 2019 brings with it the challenges and excitement of these different projects.

In November of this year the main international PWS conference will take place in Cuba, hosted jointly by the Cuban Genetics Society and the International PWS Organisation (IPWSO). Details can be found on the last page of this newsletter. I hope that some of you will be able to attend. Thank you to all of you for your interest and support and please pass on this newsletter to others. We need your help and importantly the help of people with PWS. Best wishes for the new year. 

Professor Tony Holland

Vagus nerve stimulation (VNS) project

We have completed our VNS study which looked at whether or not vagal nerve stimulation, using the Nemos device, could help people with PWS who often struggle with their behaviour. We monitored the occurrence of problem behaviours in five people who experienced frequent temper outbursts. Four out of the five people showed improvements in their behaviour which has had a transformative effect on their quality of life and also that of their families and carers. Everyone who took part in this study has chosen to continue wearing the tVNS device. We have reported the findings from this study in a manuscript which is currently under review and we hope to publish this soon.

In the VNS study using the Nemos device some participants in the early stages of the study found wearing the electrode in their ear difficult as it fell out easily. For this reason, we decided to investigate whether another nerve stimulator called Alpha-stim might have the same therapeutic effects as the Nemos device. The Alpha-stim device is easier to wear as it clips onto the ear more securely than Nemos. However, we have conducted this study in three people with PWS and found no effect on behaviour. We are now working closely with the company that produce the Nemos device to make small modifications that will make the device easier to wear.

Given the success of the Nemos VNS device in treating problem behaviours, we are currently applying for funding to conduct a larger trial. Once we gain funding, we will be looking to ask 20 people aged 12 to 50 years old with PWS who often struggle with their behaviour to wear the Nemos device for 18 months whilst we monitor their behaviour. We are also interested in investigating how VNS might work. We will look for biological mechanisms that may underpin VNS’s effectiveness (such as heart rate variability) which will allow us to see if VNS might work in people with other neurodevelopmental disorders. For example, people with Fragile X Syndrome also suffer from temper outbursts that are similar to those in people with PWS and we think VNS may be useful in treating these behaviours.

We will keep you updated with progress on our funding application and any details about a new VNS trial. For more information please contact Jessica Beresford-Webb on jb2192@medschl.cam.ac.uk

Using smartphones and wearable technologies to assess people with PWS

We have started a new research project that aims to facilitate various PWS studies through the use of smartphones and wearable devices. By using these digital technologies, we may detect people’s daily behaviours and any changes in a more accurate and timely manner, that is also easier to monitor.

Jennifer Noh, who recently joined the research group as a master’s student, is collaborating with our industrial partner, Monsenso, to develop and test this digital-based system. Recruitment of participants will start in the spring of 2019. For more information please contact Jennifer Noh on jmn52@medschl.cam.ac.uk
Investigating visual attention in infants with Prader-Willi syndrome

The characteristics of children with Prader-Willi syndrome (PWS) include impairments in social functioning, which become apparent during early childhood. Some of the difficulties are in the ability to recognise and process important visual social cues. As well as impairments in social functioning children with PWS also develop an insatiable appetite and have difficulties in shifting their attention away from food. The above observations strongly indicate impairments in both the visual and attentional abilities of children with PWS, and the potential for the development of an excessive interest in food to affect early social development.

In collaboration with Dr Victoria Leong in the Department of Psychology at the University of Cambridge, and based on findings from a pilot study undertaken in 2017, Suzannah Lester and Professor Tony Holland will be developing methods of assessing aspects of early social development of infants and young children with PWS.

By presenting images of faces, toys and food on a computer screen, our first aim is to investigate how visual attention in infants and young children with PWS, compares to typically-developing children. A second aim is to investigate at what age an increased interest in food is first observed in children with PWS, and to understand how this increased interest might impact upon their attention to other important social information, such as toys and faces, deemed critical for early social development and learning.

Suzannah Lester is currently applying for permission from the ethics committee, and once this is obtained we will be contacting the parents of infants and young children with PWS between the ages of 12 and 30 months of age.

The aim of this study is to gain an understanding of visual attention in infants and young children with PWS, and a knowledge of the age at which an interest in food increases, all of which will help inform and better evaluate early stage interventions. The long term aim of this research will be to improve early social development and learning.

For more information please contact Suzannah Lester on sl910@medschl.cam.ac.uk

Mental health study

We are currently finalising the preparation of our exciting new study investigating mental health in Prader-Willi syndrome. This study is led by Lucie Aman as part of her PhD. We will start recruiting participants in February.

The aim of this study is to better understand why some people with PWS (particularly those with UPD) have a high risk for developing mental ill-health and ultimately to be able to test treatments that might prevent the problem developing.

We will be asking people with Prader-Willi syndrome to come to our research facility in Cambridge. The participants will then be asked to wear a special cap (see the photo of Lucie wearing it!) that will record the brain activity while they listen to sounds using earphones.

The first technique described measures variations in the electrical activity of the brain. We are also working with Professors Zoe Kourtzi and Paul Fletcher and Dr Polytimi Frangou to use new brain scanning technology, again to study what brain changes put people with PWS at risk for such problems. If this is ready in time we will ask participants if they would like to do this study as well. People can choose just to do the first or they can do both.

We will also ask people with PWS to fill in some questionnaires and answer questions about their behaviour and mental health. We will also ask a parent or carer about the behaviour and mental health of the person they care for.

We will pay for the travel, food and drinks and accommodation (if needed) of the person with PWS and their carer. If you want to know more about this study, or register your interest, please email Lucie Aman on lcsa2@cam.ac.uk
Journal articles

Tony Holland and Joyce Whittington have recently published two new papers. If you would like an electronic or paper copy of either paper please contact us using the details below.


International conference on PWS in Cuba this November

The International Prader-Willi Syndrome Organisation (IPWSO) is holding its international conference in Cuba this November. The conference, which is held every three years, provides an unique opportunity for scientists, doctors, caregivers, parents, families and people with PWS to come together to share information, discuss ideas and develop new links.

For further information and to register your interest please visit [www.ipwsoconference.org](http://www.ipwsoconference.org)

Raising money for PWS research and care

Suzannah Lester is running the Cambridge half marathon in March to raise money for the Prader-Willi Syndrome Association UK. You can help her raise money for this great cause by donating directly to her fundraising page: [https://www.justgiving.com/Suzannah-Lester](https://www.justgiving.com/Suzannah-Lester).

JustGiving sends your donation straight to the Prader-Willi Syndrome Association and automatically reclaims Gift Aid if you are a UK taxpayer, so your donation is worth even more. Thank you!

Contact details and thanks

Please spread the word about these projects. None of them would be possible without the help of you all and particularly people with PWS. Thank you also to all those who have funded this work. Research is truly a collaborative and international exercise. If you would like further paper copies or to receive an electronic version of this newsletter to pass on to others please do let us know.

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