New year, new research horizons!

Since our first newsletter we have further extended the PWS Research Group here at the University of Cambridge. You can read more about this in the newsletter. This is an exciting development as it extends the expertise of the group beyond the behavioural and clinical sciences into the basic sciences and it links us more closely with the Institute of Metabolic Medicine at the Biomedical Campus on the Addenbrooke’s Hospital site. This Institute has a longstanding interest in obesity and has been among the first in the world to describe rare examples of families with identifiable genetic disorders associated with extreme forms of obesity. With the increasing complexity of science a greater range of skills and facilities are needed to address fundamental questions in disorders as complex as PWS. These include, not only expertise in the basic medical sciences, but in areas such as computer science and machine learning and, particularly with different forms of neuroimaging, the disciplines of chemistry and physics. Future newsletters will try and represent this increasing research diversity and report back on what different groups are doing.

You will see in the newsletter that the study led by Vicky Leong and Suzannah Lester of infants with PWS has started (see picture to the right). The young participants were wonderful and engaged fully with the study with support from their parents. We are very grateful for all the help and as the data comes together from this initial pilot work Vicky and Suzannah will determine how the larger study should develop. Such pilots are enormously important as they show the researchers what works and what doesn’t and allows for feedback from participants and, in this case, the families.

We are now at the stage of analysing the data from our study of the use of vagus nerve stimulation. Again, as described above, the initial pilot work has been very helpful as it indicates a likely significant beneficial effect but it has highlighted some problems with using the Nemos device. This has led us to consider a different device. It also illustrates how research is iterative and builds on observations and there are times when there are setbacks or side-way moves – what matters is that the progression is in general forward!

On the back page of this newsletter we describe how research findings are disseminated and the important role that organisations, such as the UK PWS Association and the International PWS Organisation, can play in this process. As papers are published we will list them in our newsletters and please contact Agnes if you would like a copy. As projects come to an end we will also ask those who have led them to write an article for this newsletter. If those of you with PWS who have taken part or your families or paid carers would like to write anything about the experience we would be very pleased to hear from you and to publish it in the newsletter. Please contact Agnes – she may also contact you to ask if you could help!

Thank you again for your help.

Tony Holland
Understanding early development and mother infant attachment

Over the last few months, the Baby-LINC Lab, led by Dr Vicky Leong, part of the Department of Psychology at the University of Cambridge, has commenced research investigating how interpersonal trust develops between babies and adults, and how this process might be affected by social factors such as eye-contact.

Suzannah Lester, a research collaborator, has been running the clinical aspect of the PWS Trust Pilot study, which is interested in whether children with Prader-Willi syndrome may show early differences in the development of interpersonal trust, and whether this may be related to abnormalities in the availability of the hormone called oxytocin. In collaboration with Lucie Aman, Suzannah welcomed three families who travelled to Cambridge to have their child’s brain activity recorded, which was done using wireless dual-electroencephalography (EEG) to simultaneously measure the neural oscillatory activity of infants and an experimenter, whilst engaged in a variety of tasks.

All our little participants had great fun with toys and bubbles. Suzannah and the Baby-LINC Lab are now busy analysing the data collected during these sessions. We hope this work will result in a full-scale study aiming to understand the underlying brain mechanisms that may be faulty in infants with PWS and how that relates to their early development and to the switch from under to over-eating. We will keep you updated on developments with this project.

Journal articles

We have published two new papers recently. If you would like an electronic or paper copy of either paper please contact Agnes on ah937@medschl.cam.ac.uk

More scientific collaborations to come

Several clinicians and basic and behavioural scientists based in Cambridge are undertaking or are planning to be involved in research into various aspects of Prader-Willi syndrome.

The research extends from studies using mouse models and stem cells to studies of early infant development and to adult mental health and behavioural problems in adult life and also to the ethical and legal issues with respect to limiting access to food to prevent severe obesity.

A meeting took place in December to bring these scientists together and to make everyone aware of the nature and extent of research into PWS being undertaken in Cambridge with a view to sharing knowledge, promoting inter-disciplinary working and the development of ideas and collaborations.

Vagus nerve stimulation (VNS) project

We are continuing to explore whether a device called a vagus nerve stimulator can help people with PWS to control their behaviour. This device sends small electrical impulses which activate a nerve called the vagus nerve. This nerve connects the brain and the organs in the upper body.

Five people with PWS who struggle to control their behaviour have worn the device for approximately 8-12 months with their carers recording the occurrence of difficult behaviour episodes.

Results are promising with evidence of some improvements in the ability to control behaviour which is having a positive impact on the person’s quality of life and that of their families and other carers. One problem has been that some early participants found wearing the electrode in the ear quite difficult as it easily fell out and for this reason they stopped using it and withdrew from the study. We are now investigating another stimulator called Alpha-Stim. This is also thought to stimulate the vagus nerve and has been approved for the treatment of anxiety. We have applied for ethical approval to try this device. If it also works and its use results in improvements in behaviour then it may be much easier for people to use.

We are looking for adults with PWS who have a history of difficult behaviour to help with this study so do contact us if you are interested or know of someone with PWS who may be interested. Overall the use of the original VNS seems very encouraging and we are learning more about why people with PWS might be prone to such behaviours. We will keep you updated with progress as we further analyse the data and write the paper reporting the findings. Watch this space!

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Maintaining mental health in PWS project

Lucie Aman started her PhD last October, investigating mental health and psychosis in PWS. Ethics approval has been given for a pilot study of 6 adults. Recruitment of participants will start at the end of spring 2018. In the meantime Lucie has published a paper on possible mechanisms of psychosis in PWS, details can be found on the opposite page.
From research findings to implementation

In 2006 what became known as ‘the Cooksey Report’ highlighted the difficulties in translating research findings in the laboratory to improvements in treatment and patient care [https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/228984/0118404881.pdf]. The report commented that there was much to be proud of with UK clinical science but ultimately what matters is that research leads to improvements in care. This gap between research and implementation is perhaps an even greater problem with rare disorders, such as Prader-Willi syndrome. In many countries in the world PWS may not be diagnosed and if it was suspected clinically, the genetic test may not be available. In the UK one would hope that PWS is now diagnosed early in life and with that diagnosis comes information. Organisations such as the UK PWSA (www.pwsa.co.uk) and the International PWS Organisation (www.IPWSO.org) are crucial in providing advice to new parents of a child diagnosed with the syndrome, and also as a source of ongoing support and advice. With knowledge informed support can be provided and severe obesity prevented by supervising access to food. Growth hormone replacement is recommended and available in many countries. This has meant that we are seeing a new generation of children with PWS diagnosed within days of birth and who have never been obese and are of normal stature, and their appearance is such that you would not recognise that they have PWS. These are very positive developments but there is much still to understand. How to explain this switch from under- to overeating? What is at fault which results in a failure to regulate energy intake and can that be modified through the use of medications acting on key brain pathways? How to explain the link between the complex genetics of PWS and the range of behavioural and mental health problems that are observed? There are many more questions for researchers to face.

The process from research to new treatment will depend on many factors not least funding to support research, clinicians and researchers interested in the topic, people with PWS and their families willing to help, and technologies and methodologies that allow the necessary investigations to be undertaken. As hypotheses are tested and findings peer reviewed and subsequently reported in the scientific literature so a body of evidence builds up. Sometimes the evidence emerges following a systematic approach or there may be an element of serendipity. However, a key part of this process is for all the parties involved to occasionally meet, hear from each other and exchange ideas. As described in this newsletter we are doing that in a small scale here in Cambridge. However, in the case of PWS this happens internationally every three years when, in partnership with the host country, the International PWS Organisation International Conference is held. In 2016 it was in Toronto and in 2013, Cambridge. In 2019 it is in Cuba from the 13th to 17th November. These international meetings are in English and have four components: a clinical and scientific meeting, a professional caregivers meeting, a conference for families, and events for people with PWS. The different parts of the meetings partly overlap and there is a chance for all present to meet and talk and importantly for different ideas from around the world to be shared. Please keep an eye on the IPWSO website for further details. If you decide to come, practice your Spanish and your salsa and start saving!

New team member

Jessica Beresford-Webb recently graduated from Kingston University London with a BSc (Hons) in Sociology and an MSc in Psychology. She joined the CIDDRG in November 2017 as a Research Assistant and is working on the vagus nerve project.

Contact us

Our website: www.ciddrg.org.uk
Email: a9h937@medschl.cam.ac.uk
Phone: 01223 465 216
Write: Agnes Hoctor, Team Administrator
PWS Research Group
Douglas House
18b Trumpington Road
Cambridge CB2 8AL

Thank you

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 do let us know.