



UNIVERSITY OF
CAMBRIDGE

Prader-Willi Syndrome Research Group

Newsletter

January 2020

Happy New Year!



The CIDDRG research group at Christmas

Prader-Willi Syndrome: a long journey of discovery

PWS was first described in 1956. Since that first report much has changed: families can now expect to have an early and accurate diagnosis, to be much better informed, and in many countries children with PWS will receive growth hormone supplementation thereby improving their height and body composition. The international meeting of the International Prader-Willi Syndrome Organisation (IPWSO) occurs every three years; in November 2019 it was in Cuba. The next meeting takes place in Limerick, Ireland between the 6th and 10th July in 2022. These meetings are very important as they provide the opportunity for reflection as to what has been achieved in the previous three years and, in addition, the discussion and debates that take place between everyone help to crystallise thinking as to what still needs to be done - there is much! The Cuba meeting was particularly special, I think at least partly, because the difficult circumstances and complex politics that has for my lifetime enveloped this island made all those who attended determined for the meeting to succeed and for any minor glitches to be forgotten. Whilst the presentations, particularly at the Clinical and Scientific Conference illustrated we know more, discussions with families and care providers from many different parts of the world attending the parents and care-givers conference showed that a major challenge is for the information and necessary resources to be available globally.



In this newsletter we bring you up-to-date on the research we have been doing or are linked with from the basic science to the clinical. Suzannah Lester's study of children between the ages of 12 months and three years is complete. She will shortly be examined on her Thesis and will be writing papers for publication.

Continued...

She received wonderful support from families of children with PWS and also those with typically developing children. These papers and the full findings will be available shortly. The findings from the Vagus Nerve Stimulation study using external stimulators is now published with exciting results. We are now planning the next stage. Lucie Aman, with support from Chiara Avancini, has developed her EEG methods and is now actively recruiting for her study, the aim of which is to help us understand more about the reasons for mental ill-health particularly in people with PWS due to having a maternal UPD of chromosome 15. Elena Bochukova, at Queen Mary College, London continues her investigation of the genetic and cellular abnormalities of PWS studying hypothalamic tissue and also using stem cell techniques to recreate neuronal tissue from small skin biopsies given by people with PWS. A study that is also going to involve people with PWS is that being undertaken by Jennifer Noh. This involves using smart watches and an app to monitor in real time the behaviour and physiology (activity, heart rate and sleep) of people with PWS to better understand the reasons for temper outbursts. For the analysis of the complex data that is collected in this way we are collaborating with Dina Kronhaus and Stephen Eglon in the Department of Mathematics, University of Cambridge. In partnership with Dr Elizabeth Fistein at the University of Cambridge and with IPWSO we are undertaking an extensive study to better understand the use of restrictions in the lives of people with PWS. This has involved a detailed review of the legal and clinical literature and we will shortly be undertaking a consultation with families and others across the world about your views on what is necessary and justified. We will be in contact about this study in due course.

In all these endeavours we are dependent on funding from various organisations including the Foundation for Prader-Willi Research, the Baily Thomas Charitable Trust, the UK PWSA, and from Sam's Foundation. Thank you to all of them. We are also completely dependent on the willingness of people with PWS to take part and to families and paid care providers for their help answering questions and bringing people to Cambridge. Thank you for your support. If you wish to know more about these studies or to help with any of the ones still on-going please contact us.

Professor Tony Holland

PWS Research

Investigating the Allocation of Visual Attention to Salient Stimuli in Infants and Young Children with Prader-Willi syndrome

Suzannah Lester's study was completed in December, and will be submitted for publication early next year.

Suzannah's study aimed to better understand the switch from under eating to over eating, known to occur during early childhood. 10 children with PWS aged between 11 and 30 months and 20 age matched typically developing children took part. The study used visual imagery presented on a screen to assess how the infants allocated their attention towards emotional images (faces), food images,



PWS Research continued...

and perceptual images (coloured objects), to examine if infants and children with PWS showed a bias in their attention towards the food stimuli. The Early Social Communication Scales provided an insight into the social communication abilities of the PWS infants, who all seemed to really enjoy this! This study is the first of its kind to provide an understanding of how infants and young children with PWS allocate their attention towards important environmental stimuli, and delivers critical insight as to the salience of food images during early life. In addition, the use of observational measures of non-verbal social interaction has provided an understanding of how infants and young children with PWS socially interact and communicate.

Suzannah would like to issue a huge THANK YOU to all the incredible families who took part in the research. Thank you also to those who wanted to take part but were not able to at the time. The support we received was unprecedented, and we cannot express our thanks enough. **We look forward to sharing our findings in the New Year!**

Psychosis in Prader-Willi Syndrome

This study is now recruiting!

Thanks to the help of the Consensus Support group in Northamptonshire we have now recruited 6 participants with PWS, and will be recruiting more participants later this year, starting in April.

We will be asking people to come to Cambridge and have their brain activity recorded while they listen to sounds. We will also ask people to do some puzzles and games, and answer questionnaires. We will pay for all travel costs and overnight accommodation if needed.

If you want to know more, email Lucie (lcsa2@cam.ac.uk), she will then send you an information pack.

Welcome to Chiara Avancini who will be joining the team for a few months to help Lucie with the brain recording technique EEG.



Using Smartphones and Smartwatches to Assess People with PWS



This study is now recruiting!

We are looking for people with PWS who are 12 years of age or older.

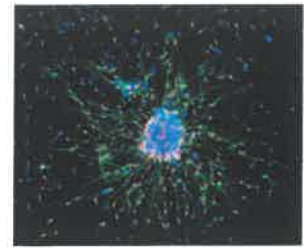
In this exciting new strand of research, we will be asking participants (who have PWS) and their caregivers to complete the daily self-assessment questionnaire through their own mobile phones and to wear a health-tracking smartwatch on a daily basis. We wish to undertake this study for 2 months, but it will depend entirely on the participants if they wish to end the study earlier. For the initial meeting, participants can either choose to visit our laboratory in

Cambridge, where all travel costs will be covered, or we could visit the participants with appointment.

If you want to know more about this study or interested in taking part, please send email to Jennifer (jmn52@medschl.cam.ac.uk), she will be very happy to answer any questions.

Investigating Prader-Willi neurodevelopment in stem cell models

Elena Bochukova's research on Prader-Willi is aimed at understanding the molecular events and cellular function that is changed or compromised in the patients' brain cells. To achieve that, her team is utilizing precious stem cells, derived from patients' skin (kindly gifted from Prof Rick Livesey's group in Cambridge), which they make into brain cells (neurons) in the lab.



Experiments undergoing in the lab are focusing on **comparing the stem cell-derived neurons from the patients to these from healthy controls**. They focus on changes in neuronal cell properties and behaviour, for example neuronal migration, which is a crucially important characteristic of neurons in the developing human brain. The picture includes an example of neurons from a patient, grown 'in a dish'. Shown labelled in green, the neurons start moving and researches could measure their migration under the microscope. These techniques provide and an unparalleled opportunity to study developing patients' neurons directly, which are otherwise inaccessible.

They also use the stem cells differentiated into neurons, to try to understand **which genes are deregulated** in the condition. Previously Dr Bochukova's lab looked into gene expression changes in donated patients brain samples, and highlighted compromised neuronal survival, compared to healthy controls. Now, her group is trying to discover what makes the patients neurons vulnerable, the precise molecular changes that take place in the patients cells, and understand how these changes could guide future therapies for Prader-Willi syndrome.

Stay Calm Project

We would like to bring to your attention a research project that is being conducted at the School of Psychology in the University of Birmingham, UK. The **Stay Calm** project is being led by Justin Chung, under the supervision of Dr Kate Woodcock.

This project aims to develop and evaluate an informant-report questionnaire, which will be used to assess the characteristics of emotional outbursts in more detail compared to existing measures. This will be a valuable tool for researchers and clinicians in future. It will allow valuable information to be obtained quickly, which may contribute to our understanding of the cognitive, emotional, and neurobiological underpinnings of emotional outbursts and be particularly important when developing new treatment strategies. We are focusing on emotional outbursts because we understand that they can be a particularly significant problem for some families.

We are specifically looking for parents and caregivers of individuals between the ages of **6 years old to 25 years old, who have emotional outbursts at least once a month**. We are interested in collecting anonymous questionnaire responses from parents and caregivers online.

The questionnaire can be accessed via the following link:

https://bhampsiychology.eu.qualtrics.com/jfe/form/SV_25dCk3mw4PS3Q8t

Alternatively, you can visit our project webpage, which contains a link to the questionnaire, as well as some basic information about the research:

<https://www.katewoodcock.com/staycalm/>

We anticipate that the questionnaire will take no more than 1 hour to complete (most likely around 30 minutes).

IPWSO's 10th international conference, Havana, Cuba



IPWSO holds an international conference every three years in collaboration with a local host. They have been working with the Cuban Society for Human Genetics since the conference was awarded to Havana at the previous IPWSO conference in 2016, to organise a PWS conference for professionals, caregivers and families to be conducted in English and Spanish for delegates from around the world. The conference was one of the most dynamic and diverse of

recent years with almost 500 delegates from 43 countries, including 200 from Cuba itself. Agnes, our former team administrator now working full time for IPWSO, has been working very hard to make this event happen.

The programme was split into four sections:

Clinical and Scientific, Professional Providers and Caregivers, Parents and Activities for People with PWS. A particularly strong Scientific programme was praised by many delegates who left conference empowered with new knowledge and ideas. Presentations were given by established scientists as well as those at an earlier stage of their careers on topics including mouse models, nutrition, clinical trials, hyperphagia, orthopaedics and many other areas.

During the conference, Tony Holland chaired a session on clinical trials for hyperphagia at the scientific and the professional providers and caregivers' conferences. As part of his project with Elizabeth Fistein, Tony also spoke about legal and ethical basis for restrictions to freedom in order to limit access to food.



Together with Janice Foster Tony also spoke about behaviour and mental health at the parent's conference. This session was in the form of a dialogue discussing how such problems are recognised, diagnosed and best managed. There were four posters from Cambridge. Lucie Aman presented a poster about her research on psychosis in PWS. Suzannah couldn't attend in person, but had a poster on display with exciting results from her master project on visual attention in young children with PWS. The two

other posters were part of a project being led by Dr Elizabeth Fistein on the ethics and legality of using restrictions on a person's freedom to control access to food. These posters were systematic reviews of the scientific literature on the risk of obesity related illness and mortality in people with PWS and on what treatments and managements strategies were being used to prevent obesity.



IPSWO Conference continued...

IPWSO awarded travel grants to exceptional candidates from around the world who would have been unable to attend the conference without financial assistance. This included delegates from Argentina, Bulgaria, Columbia, El Salvador, Georgia, India, Kenya, Mexico and South Africa.

November was also a special time for the city of Havana as the city celebrated its 500th year and there were street parties and fireworks to celebrate. More information: <https://www.ipwso.org/conferences>

IPWSO Project ECHO

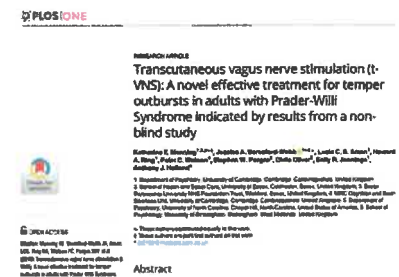
At the General Assembly in Cuba a new Board was elected. Tony continues as President for a further three years. As part of future plans IPWSO is developing a project first started at the University of New Mexico, Albuquerque, USA called 'Project ECHO'. This project uses zoom based technology to spread knowledge on complex disorders. It uses the principles of 'case-based' learning and seeks to develop best practice in remote areas. Three people from IPWSO have attended the ECHO Institute and IPWSO is now in the process of establishing PWS ECHOs to bring our membership together and to develop best practice in countries where knowledge about PWS is limited.



Journal articles

The article about our research on vagus nerve stimulation to help with temper outburst in PWS is out now. We would like to thank our participants, their family and carers. This study used an externally worn stimulator and was investigating whether treatment using VNS worn four hours each day over many months helped behaviour. Considerable improvements were reported. Further trials are being planned.

You can find it here: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0223750>



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.

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Sam's PW Research Foundation

