10th INTERNATIONAL PRADER-WILLI SYNDROME ORGANISATION CONFERENCE

13-17 NOVEMBER 2019 HAVANA, CUBA

SOCUGEN
Sociedad Cubana de Genética Humana

IPWSO
INTERNATIONAL
PRADER-WILLI SYNDROME
ORGANISATION

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INTERACTION Empowering People with PWS

pwsa prader-willi syndrome association VIC

WELCOME TO HAVANA!

Welcome to the 10th International Prader Willi Syndrome conference hosted by the International Prader-Willi Syndrome Organisation (IPWSO) in partnership with the Cuban Human Genetics Society (SOCUGEN). Welcome also to Cuba with its rich history, music and culture!

Cuba was chosen to host this conference by the IPWSO general assembly at the 2016 IPWSO meeting held in Toronto on the initiative of Loisel Bello Ulloa and Marlen Román García, who have a daughter with PWS, with the strong encouragement of Giorgio Fornasier. Since then Cuba has gone on to develop its diagnostic services for people with PWS and families are now coming together to share their experiences and to support each other.

Our conference has expanded over the years and again we are holding Clinical and Scientific, Professional Providers' and Caregivers', and Parents' Conferences together with meetings and activities for people with PWS. In these different conferences there will be clinicians, scientists, researchers, family members, representatives from industry, and professional caregivers presenting and discussing new discoveries, and describing their experiences. Speakers and attendees come from many different countries - this is your opportunity to hear from and talk to those engaged in research, to share ideas with families and caregivers from across the world, and to meet with clinicians.

This will be the first of our international conferences to be held in a Spanish speaking country and to be located close to Central and South America and we believe that having the meeting here in Cuba has already encouraged national associations in these parts of the world to expand their work. As you will hear this week our understanding of PWS continues to advance and we are now at a stage where new treatments are being tested in clinical trials. The importance of good and informed support with the presence of food security is also now recognised in many countries. However, we also know that there are many countries with very limited support and with few professionals who understand PWS. These conferences are therefore not only about sharing ideas and new knowledge but also about spreading that knowledge across the globe so that all people with PWS can have a good life.

These conferences take a lot of organisation and we would like to thank numerous people in IPWSO and in Cuba who have been working away behind the scenes on a voluntary basis to make this meeting possible. We would also like to thank the management of the Cojimar Conference Centre for hosting us this week and helping us plan this meeting and the staff of Solways and Havanatur.

Finally, we want you to go away from Cuba having had a very special experience both in terms of understanding PWS just that little bit more but also having had a chance to see Havana and other parts of this beautiful island. Havana is celebrating its 500th anniversary as a city during our conference, so it is truly a special time to visit.

IPWSO
INTERNATIONAL PRADER-WILLI SYNDROME ORGANISATION

PROFESSOR TONY HOLLAND
President IPWSO

SOCUGEN
Sociedad Cubana de Genética Humana

DR BEATRIZ MARCHECO TERUEL
President, the Cuban Society for Human Genetics

ABOUT THE INTERNATIONAL PRADER-WILLI SYNDROME ORGANISATION (IPWSO)

We have been in existence for almost 30 years and were formed by Jean Phillips-Martinsson (our Honorary President) from Sweden, Henk Mozelaar from Holland, and Suzanne Cassidy from the USA. Their wish to hold an international conference on Prader-Willi syndrome came to fruition in 1991 in a small town in The Netherlands and IPWSO was born.

Our aim has always been to support families around the world by providing knowledge, information and support. We hold three-yearly conferences where scientists, researchers, medical personnel, families and those with PWS can come together; we support the building of new Associations around the world; and fund free diagnosis (this came a little later with an introduction by Giorgio Fornasier, then President, to the BIRD Foundation in Italy).

Big plans, far-reaching, and maybe idealistic, but definitely achievable! We now work with over 100 countries around the world, have reached our 10th international conference and have supported many countries to hold their own national conferences.

Since our last conference in Toronto in 2016 we have supported workshops and conferences in Morocco, Colombia, Vietnam, Chile and Bulgaria as well as the Asian Pacific PWS conference in Australia. We have worked tirelessly to make this conference happen in Cuba, and look forward to supporting other country workshops and conferences over the next three years. We also host information booths at educational conferences run by other networks where we disseminate information about PWS to groups including endocrinologists, psychiatrists and medical researchers.

Our specialist Boards have continued to provide amazing support to families and professionals. We have answered many emails requesting medical help and information and consulted our Clinical and Scientific Advisory Board who have given willingly of their time and knowledge. The Board has also produced valuable guidance documents which are available on our website. Our Professional Providers and Caregivers Board has also produced important guidelines and run conferences most recently in Munich in 2018.

Funding free diagnostic testing for PWS for people living in countries where this is not available is an extremely important part of our work. Working with the BIRD Foundation in Italy we have now funded the testing over 500 samples from 45 countries and we know the real impact these diagnoses have for the families concerned.

Every three years at our international conference we hold our General Assembly, an important part of our constitution. At the General Assembly (which takes place at 5pm this Sunday) our member countries vote for new candidates for the Board. This year we have six of our nine members retiring after serving two terms of three years. We bid a fond farewell to our extremely hard-working Vice President, Marguerite Hughes (Ireland), our diligent Treasurer, Hubert Soyer (Germany), amazing Secretary Marilyn Dumont-Driscoll (USA), and our wonderful board members Mariona Nadal (Spain) and June-Anne Gold (USA), as well as our dedicated head of our Famcare Committee, Georgina Loughnan. You have all served IPWSO so well and we will miss you! We wish you all the best in your careers, or retirement, and thank you for your contributions over these past six years. With your tremendous help and support we have achieved the goals we set for ourselves and on which we will continue to build. We are also very sadly saying goodbye to Linda Thornton as she retires from her central role with us (see separate page for a tribute to Linda).

HOW TO SUPPORT US

The key role of IPWSO is to support families in countries where information and support is lacking. Our conference helps bring together many parts of the international PWS family and helps spread the word about new developments across the world. We can't do this without your support. Please do consider supporting us with a donation, this can be done online (as a one off or as a regular payment) at www.ipwso.org

THANK YOU!

ORGANISING COMMITTEES

CENTRAL COMMITTEE:

1. Prof. Tony Holland, Co-President of the Conference, President of the International Prader-Willi Syndrome Organisation (IPWSO)
2. Beatriz Marcheco Teruel MD, PhD, Co-President of the Conference, President of the Cuban Human Genetics Society
3. Dra. Yaíma Zúñiga Rosales, Cuban Human Genetics Society
4. Dr Marguerite Hughes, IPWSO Vice-President

CLINICAL AND SCIENTIFIC COMMITTEE:

1. Daniel J. Driscoll, MD, PhD, Professor of Pediatrics and Genetics. Chair of the Clinical and Scientific Advisory Board of IPWSO.
2. DraC. Prof. Estela Morales-Peralta, Clinical Geneticist. Board Member of the Cuban Human Genetics Society.
3. Dra. Hilda Roblejo Balbuena MsC., Clinical Geneticist. Member of the Cuban Human Genetics Society.

PROFESSIONAL PROVIDERS' AND CAREGIVERS' COMMITTEE:

1. Norbert Hodebeck-Stuntebeck, PhD, Psychologist. Chair of the Professional Providers and Caregivers Board of IPWSO.
2. Dra. Beatriz Suárez Besil, MsC. Genetics Counsellor. Member of the Cuban Human Genetics Society.
3. MsC. Damaris Rizo López, MsC. Genetics Counsellor. Member of the Cuban Human Genetics Society.

PARENTS' COMMITTEE:

1. Amalia Balart, Board member, IPWSO
2. Verena Gutmann, Board member of IPWSO
3. Georgina Loughnan, Director FAMCARE, IPWSO
4. DraC. Prof. Paulina Araceli Lantigua Cruz, MD, PhD. Clinical Geneticist. Vice-President of the Cuban Human Genetics Society.
5. Dra. Laritza Martínez Rey, Clinical Geneticist. Member of the Cuban Human Genetics Society

PEOPLE WITH PWS COMMITTEE:

1. Dr. Loisel Bello Ulloa, MsC.
2. MsC. Marlen Román García, MSc.
3. Maylin Armas Fuego. Local Coordinator of CARITAS-CUBA.
4. Mariona Nadal, Board member of IPWSO
5. Daniela Rubin, PhD, California State University, Fullerton, USA.

LOCAL INFORMATION AND EMERGENCY NUMBERS

PHONE NUMBERS

Cuba country code: +53
In a medical emergency call: 104
To call the police: 106
To call the fire department: 105

TAXI COMPANIES

Cuba taxi: +53 7835 5555
Or find a private taxi outside the hotels.

RESTAURANTS

Ask the concierge at your hotel for local suggestions. TripAdvisor.com also has many suggestions including reviews of the restaurants below which have been suggested by our local hosts.

RESTAURANTS NEAR THE NACIONAL HOTEL:

- Mediterraneo, Between F and G 13 St, #406, Vedado, Havana 10400, Cuba. (+53 7832 4894)
- Café Laurent, Calle M # 257, 19 y 21 Vedado, Havana 10400, Cuba. (+53 7831 2090)
- Los Amigos, Calle M No 253, Vedado, Havana, Cuba. (+ 53 830 0880)
- La Rambla, Calle L Numero 310, Havana 10400 Cuba. (+53 5818 6947)
- La Roca, Calle 21 esq. a M, Havana Cuba. (+53 733 4501)
- There are also two restaurants that operate inside the Nacional hotel, La Barraca and La Veranda (buffet).
- At the Habana Libre hotel there is a restaurant called Polinesio (in the basement).

RESTAURANTS NEARER THE CONFERENCE VENUE IN COJIMAR:

El Cojimero, Calle Morro # 8644 e/ G y H. Cojimar, Cojimar, Cuba. (+53 7766 6724)
Casa Grande, Pezuela 86, Esquina Foxa, Cojimar, Cuba. (+53 5316 6295)
Las Terrazas de Cojimar, Calle 152 #161, Cojimar, Cuba. (+53 7 7665151)

GROCERIES

For groceries near the hotels: Palco, Galerías Paseo, Carlos III, 3ra y 70, 5ta y 42.
There is a grocery shop in the basement of the Nacional hotel.
There is a gallery of shops in the Habana
Libre hotel.
Shops in La Rampa area are also near
the main hotels.

TOURS

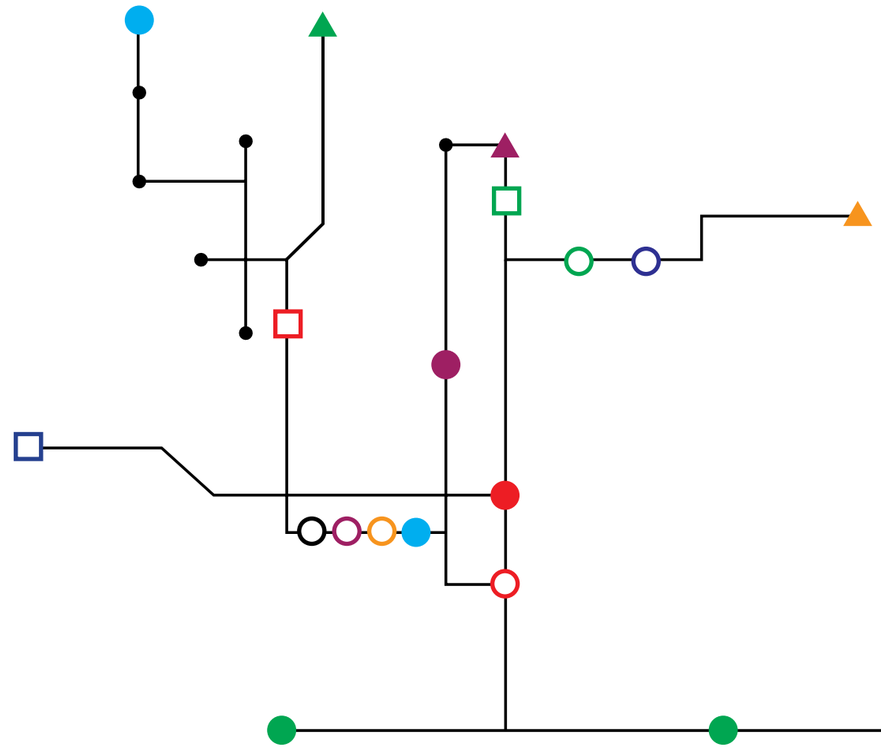
Please contact Grisel or Caridad from Havantur who will be delighted to book you onto a tour, various options are available.
Grisel: rpte1.eventos@havanatur.cu
Caridad: esp2.eventos@havanatur.cu
www.havanatur.cu

OUR CONFERENCE VENUE

THE COJIMAR CONERENCE CENTRE

Centro de Convenciones y Servicios Académicos Cojímar, Calle 7ma A e/ 78 y 7ma, Cojimar, Habana del Este, La Habana, 10900, Cuba. *https://goo.gl/maps/qPkeXyw25XWvtk6f8*

ROOM PLAN



LEGEND

- ENTRY
- PARKING
- BATHROOMS
- WIFI AREA
- STAIRS
- STORE
- POLIVALENTE ROOM
- THEATRE
- EXIBITION HALL
- SALÓN MARTÍ ROOM
- PROTOCOLO ROOM
- VILMA ESPÍN ROOM
- MÁXIMO GÓMEZ ROOM (ORGANIZING COMMITTEE)
- ANTONIO MACEO ROOM (REGISTRATION)
- BOLIVAR MARTÍ ROOM
- COMPLEJO EL LIBERTADOR ROOM
- SALÓN CHE GUEVARA (2ND FLOOR)

IPWSO 10TH INTERNATIONAL CONFERENCE AT A GLANCE

WEDNESDAY 13TH TO SUNDAY 17TH NOVEMBER 2019
AT THE COJIMAR CONFERENCE ENTRE,OUTSIDE HAVANA, CUBA

ALL MEETINGS ARE AT THE CONFERENCE CENTER APART FROM THE CONCERT ON SATURDAY EVENING

WEDNESDAY 13 NOVEMBER

MORNING: BOARD MEETINGS

- 13.00 – 14.00: Lunch
- 14.00 – 17.00: Roundtable on gonadal function, puberty, sexuality and fertility in people with PWS, The Theatre
- 16.00 – 18.00: Registration opens and set up of posters
- 18.00: Pfizer Welcome ceremony, Sala Polivalente

THURSDAY 14 NOVEMBER

- 08.00 – 08.30: Registration
  Clinical and Scientific programme, The Theatre
  Professional Providers' and Caregivers' programme, The Ché Guevara room
- 12.00 – 13.00: Lunch and Clinical and Scientific poster viewing
- Afternoon: Clinical and Scientific programme
- Professional Providers' and Caregivers' programme
- 17.00 – 18.00: Clinical and Scientific Poster presentations

FRIDAY 15 NOVEMBER

- 08.00 – 08.30: Registration
  Clinical and Scientific programme, The Theatre
  Professional Providers' and Caregivers' programme, The Ché Guevara room
- 12.00 – 13.00: Lunch and Clinical and Scientific poster viewing
- 12.30 – 13.00: Professional Providers' and Caregivers' poster presentations
  Afternoon: Clinical and Scientific programme
  Professional Providers' and Caregivers' programme
- 16.00 – 18.00: Clinical and Scientific Poster presentations
- 18.00 – 18.30: Latin-American Network of Specialists in PWS event, room TBC
- 18.30: Millendo Therapeutics Gala, Sala Polivalente

SATURDAY 16 NOVEMBER

- 08.30 – 09.00:Registration
  Parents' and families' programme, The Theatre
  Activities for people with PWS, Complejo El Libertador
- 12.30 – 13.30: Lunch
  Afternoon: Parents' and families' programme
  Activities for people with PWS
- 19.00: Concert, Teatro América (external venue)

SUNDAY 17 NOVEMBER

- 08.30 – 09.00: Registration
  Parents' and families' programme, The Theatre
  Activities for people with PWS, Complejo El Libertador
- 12.30 – 13.30: Lunch
  Afternoon: Parents' and families' programme
  Activities for people with PWS
- 17.00: IPWSO General Assembly, The Theatre
  Conference closes

WEDNESDAY 13TH NOVEMBER 2019, FROM 14.00 TO 17.00, THE THEATRE AT THE COJIMAR CONFERENCE CENTRE

Roundtable on gonadal function, puberty, sexuality and fertility in people with PWS hosted by the Clinical and Scientific Advisory Board and the Professional Providers and Caregivers Board of IPWSO and led by Urs Eiholzer, Center for Pediatric Endocrinology Zurich

Many children and adults with PWS have impaired sexual development due to gonadal (testes or ovaries) hypofunction as a consequence of insufficient stimulation from the hypothalamus. Standard treatments are generally available to normalize the levels of sex hormones with the aim of achieving normal puberty, libido and fertility, as well as normalizing sex hormone-dependent metabolic processes. Since about the year 2000, adolescents and adults with PWS have been treated with sex hormones, however, often at significantly subnormal doses. There appears to be a subliminal fear that replacement of the missing sex hormones will provoke aggressive behavior, mood changes, mental disorders or problems as a consequence of developing sexuality.

At this roundtable, as part of an audience discussion, all aspects will be considered as pubertal development is not only about hormonal change but it is also an important social process. We want to share the experience you have had with and without the substitution of sex hormones for people with PWS and how treatment may have influenced mood, behavior and/or sexuality. What are the advantages and disadvantages of the hormones used, the doses prescribed, at which age to start and with which formula? Experience has shown that people with PWS talk about romantic feelings and like cuddling but real sexual intercourse is probably rare – perhaps even less common among men than women with PWS. Sexuality also should not be burdened by a possible pregnancy. That is why this roundtable is also about fertility and contraceptive issues. Only a few pregnancies in women with PWS are known. Which is the best contraceptive method for PWS woman/ men? What about consent and are there risks of exploitation and abuse? Here, too, on all these matters we would like to hear of your experience.

The roundtable is aimed primarily at professionals and caregivers, attendance can be booked prior to the conference via the registration website.

CLINICAL AND SCIENTIFIC CONFERENCE: PROGRAMME

THE CONFERENCE WILL BE HELD IN THE THEATRE

THURSDAY 14TH NOVEMBER

- **08.00 – 08.30: Registration**
- **08.30 – 08.45: Introductions** Chair: Daniel J. Driscoll, University of Florida College of Medicine Co-Chair: Estela Morales Peralta, Medical University of Havana
- **08.45 – 10.00: I. Genetics, Epigenetics & Animal Models** Moderator: Suzanne Cassidy, University of California, San Francisco
- **08.45 – 09.30: I-1. Invited Talk: "Genetics in PWS:** Where We Have Been and Where We are Going" Daniel J. Driscoll, University of Florida College of Medicine
- **09.30 – 10.00: I-2. Invited Talk: "An Update on Mouse Models of PWS"** Jim Resnick, University of Florida College of Medicine. The Zafgen lecture
- **10.00 – 10.30: Break**
- **10.30 – 12.00: II. Endocrinology** Moderator: Urs Eiholzer, Center for Pediatric Endocrinology Zurich
- **10.30 – 11.00: II-1. Invited Talk: "Oxytocin in Prader-Willi Syndrome"** Maïthé Tauber, Université Paul Sabatier Toulouse 3 and Hôpital des enfants CHU
- **11.00 – 11.30: II-2. Invited Talk: "An Overview of Endocrinology in Adults with PWS"** Charlotte Höybye, Karolinska University Hospital and Karolinska Institute The Levo Therapeutics lecture
- **11.30 – 11.45: II-3. "Central adrenal insufficiency is rare in adults with Prader-Willi syndrome"** Anna Rosenberg, Erasmus University Medical Center
- **11.45 – 12.00: II-4. "Systemic Inflammation and The Effect of a GLP-1 Receptor Agonist in Adults with Prader-Willi Syndrome"** Jarron Dodds, Garvan Institute of Medical Research and University of Notre Dame
- **12.00 – 13.00: Lunch and poster viewing**
- **13.00 – 14.30: II. Gastrointestinal & Nutrition** Moderator: Maïthé Tauber, Université Paul Sabatier Toulouse 3 and Hôpital des enfants CHU
- **13.00 – 13.30: III-1. Invited Talk: "Comprehensive Overview of Digestive Issues in Prader-Willi Syndrome"**Ann Scheimann, Johns Hopkins School of Medicine
- **13.30 – 13.45: III-2. "Review of Short and Long-Term Outcomes of Bariatric Procedures in Prader-Willi Syndrome and Other Hyperphagic Disorders"**Ann Scheimann, Johns Hopkins School of Medicine
- **13.45 – 14.00: III-3. "Long-acting GLP-1 agonist treatment in Prader-Willi Syndrome: Benefits on appetite, behaviour and cognition versus risks?"**Amanda Hor, Garvan Institute of Medical Research, St Vincent's Hospital and University of New South Wales
- **14.00 – 14.15: III-4. "Effect of macronutrient composition on postprandial metabolism in children with Prader-Willi syndrome (PWS): preliminary findings"**Maha Alsaif, University of Alberta
- **14.15 – 14.30: III-5. "Relationship between Angiopoietin-like levels and non-alcoholic fatty liver disease in children with Prader-Willi Syndrome"**Antonio Crinò, Bambino Gesù Children's Hospital, Research Institute, Palidoro (Rome)
- **14.30 – 15.00: Break**
- **15.00 – 17.00: IV. General Medical Issues** Moderator: Charlotte Höybye, Karolinska University Hospital and Karolinska Institute

- **15.00 - 15.30: IV-1. Invited Talk: "Overview and Evaluation: Infants, Children, Adolescents and Adults with PWS"**Susanne Blichfeldt, The Danish Prader Willi Association and Centre for Rare Diseases
- **15.30 – 16.00: IV-2. Invited Talk: "Medical care for Patients with PWS at the National Network of Medical Genetic Services in Cuba"**Estela Morales Peralta, Medical University of Havana
- **16.00 – 16.15: IV-3. "Incidence and Consequence of Laryngomalacia in Infants with PWS seen at Seattle Children's PWS Clinic"**Parisa Salehi, Seattle Children's Hospital, University of Washington
- **16.15 – 16.30: IV-4. "Increased bone density without changes in bone markers in youth with and without PWS who participated in a 24-week physical activity intervention"**Daniela Rubin, California State University, Fullerton
- **16.30 – 16.45: IV-5. "Is There a 'Fetal Phenotype' of Prader-Willi Syndrome?"**Jude P. Crino, University of Maryland School of Medicine
- **16.45 – 17.00: IV-6. "Challenges in medical management of obesity hypoventilation in Prader-Willi syndrome"**Linda Gourash, Pittsburgh Partnership
- **17.00 – 18.00: Poster presentations, session # 1**

FRIDAY 15TH NOVEMBER

- **08.00 – 08.30: Registration**
- **08.30 – 10.00: V. General Medical Issues including Orthopaedics** Moderator: Ann Scheimann, Johns Hopkins School of Medicine
- **08.30 – 09.00: V-1. Invited Talk: "The Orthopaedics of Prader-Willi Syndrome"** Harold J. P. van Bosse, Shriners Hospital for Children
- **09.00 – 09.15: V-2. "Role of Body Cast Application for Scoliosis Associated with Prader-Willi Syndrome"**Harold J. P. van Bosse, Shriners Hospital for Children
- **09.15 – 09.30: V-3. "High prevalence of scoliosis in a large cohort of patients with Prader-Willi syndrome"** Antonino Crinò, Bambino Gesù Children's Hospital, Research Institute, Palidoro (Rome)
- **09.30 – 09.45: V-4. "Comparative Comorbidity Burden Among Patients With Prader-Willi Syndrome: A Population-Level Cohort Study"** Diane Stafford, Stanford University
- **09.45 – 10.00: V-5. "US prevalence & mortality of Prader-Willi syndrome: A population-based study of medical claims"** Shawn E. McCandless, University of Colorado
- **10.00 – 10.30: Break**
- **10.30 – 12.00: VI. Clinical Trials for Hyperphagia and Behaviour** Moderator: Anthony Holland, University of Cambridge
- **10.30 – 11.15: VI-1. Invited Talk: "An Overview of Clinical Trials"** Nathalie Kayadjanian, PWS Clinical Trial Consortium
- **11.15 – 11.30: VI-2. "Tesomet - a new treatment opportunity in Prader Willi Syndrome. Results from Phase 2a exploratory studies in adult and adolescent patients"** Dóra Török, Semmelweis University
- **11.30 – 11.45: VI-3. "Trial-in-Progress: ZEPHYR, a Pivotal Phase 2b/3 Randomized, Placebo-Controlled Study of Livoletide, a Novel Unacylated Ghrelin Analogue, for the Treatment of Hyperphagia and Food-Related Behaviors in Patients With Prader-Willi Syndrome"** Vivian H. Lin, MD, Millendo Therapeutic
- **11.45 – 12.00: VI-4. "Effect of topiramate on eating behaviours in Prader-Willi syndrome"**Sophie Çabal-Berthoumieu, Centre de Référence du Syndrome de Prader-Willi and Hôpital des Enfants, Toulouse

- **12.00 – 13.00: Lunch and poster viewing**
- **13.00 – 14.30: VII. Mental Health, Behaviour & Cognition #1** Moderator: Susanne Blichfeldt, The Danish Prader Willi Association and Centre for Rare Diseases
- **13.00 – 13.30: VII-1. Invited Talk: "Mental Health and Behavior in PWS"** Janice L. Forster, Pittsburgh Partnership
- **13.30 – 13.45: VII-2. "Cognitive functioning in children with Prader-Willi syndrome during 8 years of growth hormone treatment"**Anita Hokken-Koelega, Dutch Growth Research Foundation and Erasmus University Medical Centre/Sophia Children's Hospital
- **13.45 – 14.00: VII-3. "A Genotype-Phenotype Analysis of the Effects of Growth Hormone Treatment on Psychiatric Behavior in Prader-Willi Syndrome"** June-Anne Gold, University of California, Irvine
- **14.00 – 14.15: VII-4. "Gray matter microstructural alteration of the brain in individuals with Prader-Willi syndrome: a 7T MRI study"**Kenichi Yamada, University of Niigata
- **14.15 – 14.30: VII-5. "Bilingualism and Executive Control: the PWS population on the spotlight and... doing well"** Estela García Alcaraz, University of Ottawa and Juana Muñoz Liceras, University of Ottawa and Universidad Nebrija, Madrid
- **14.30 – 15.00: Break**
- **15.00 – 16.00: VIII. Mental Health, Behaviour & Cognition** #2 Moderator: Janice L. Forster, Pittsburgh Partnership
- **15.00 – 15.15: VIII-1. "Flexible scheduling to prevent the development of disabling resistance to change: acceptability and feasibility of a digital intervention co-produced with stakeholders"** Siobhan Blackwell, University of Birmingham
- **15.15 – 15.30: VIII-2. "A randomised control trial to evaluate the impact of engagement with a task switching training computer game on people with Prader-Willi syndrome"** Kate Woodcock, University of Birmingham
- **15.30 – 15.45:VIII-3. "Specific features in the expression of emotions in children with Prader-Willi syndrome : What are the consequences for emotion abilities and social adjustment?"** Nawelle Famelart, University of Toulouse
- **15.45 – 16.00: VIII-4. "PRACOM 2 project: Study of the emotional aspects associated to behavioral and cognitive troubles in the Prader-Willi Syndrome"**Anna-Malika Camblats, Université de Bordeaux
- **16.00 – 18.00: Poster presentations, session #2**

CLINICAL AND SCIENTIFIC CONFERENCE: SPEAKERS AND MODERATORS

MAHA ALSAIF, UNIVERSITY OF ALBERTA. *alsaif@ualberta.ca*

Maha Alsaif is currently a PhD student at the University of Alberta. She completed her Bachelor of Science degree in Human Nutritional Sciences and Dietetics Internship at (King Saud University and Al-Iman General Hospital) in Saudi Arabia. She later moved to Canada to pursue her Master of Science degree in Human Nutritional Sciences at the University of Manitoba. Her research aim is to understand the excessive weight gain in children with Prader-Willi syndrome.

SIOBHAN BLACKWELL, UNIVERSITY OF BIRMINGHAM. *S.Blackwell@bham.ac.uk*

Siobhán is a Research Associate with the Kate woodcock Research Group, under Dr Kate Woodcock. She is responsible for coordinating the 'Flexible Scheduling' Project. This project is a feasibility and acceptability study which aims to develop an intervention to prevent the development of disabling emotional and behavioural responses to change in groups considered at-risk (autism, Prader-Willi and fragile-X syndromes).

Siobhán completed her Masters in Psychological Science and her undergraduate degree in psychology at University College Dublin, Ireland. Since graduating in 2014, Siobhán has worked in research across various Higher Education Institutions, both in Ireland and England. Her core interests are in developmental psychology. Prior to moving to the UK, Siobhán held the position of Assistant Head Teacher in an early intervention centre for children with autism, as well as a teaching post on two undergraduate modules (Human Development and Psychological Assessment) for the Irish College of Humanities and Applied Sciences.

SUSANNE BLICHFELDT, MD, THE DANISH PRADER WILLI ASSOCIATION AND CENTRE FOR RARE DISEASES, DENMARK. *s.blichfeldt@dadlnet.dk*

Pediatrician (pediatric neurology, general and developmental pediatrics). Work: more than 30 years of experience with diagnoses and clinical treatment of children with PWS, incl GH treatment at University Hospitals in Denmark. Clinical advisor concerning treatment of adults with PWS. Research: GH treatment of children with PWS. Scandinavian study that led to the general recommendation of GH treatment for children with PWS in Europe in 2000. Presentations and teaching: since 1988 many teaching sessions for caregivers, teachers, parents about PWS in DK, Norway, Sweden, Finland and presentations in England, Ireland, France, Italy, Greenland, Romania and Bulgaria about various subjects in PWS incl living facilities and general medical questions. PWS in DK: Co- founder of the Danish association 1986, since 1990 leader of the advisory board in the association. Publications about PWS leaflets about various subjects, 4x times yearly articles on medical questions in The DK PWS newsletter. IPWSO related: Involved in IPWSO work since it started in 1991. Co-organizer of parent programs for several IPWSO congresses since the first meeting in 1991. IPWSO board member 2001-2004. member of PPBC 2010-2014. Advisor in CSAB since 2004, here we have the last years created our Overview and Evaluation overviews, and we serve as a group as medical advisors for parents and professionals all over the world. Presentations on various medical subjects at the IPWSO conferences especially in the programs for parents and other professionals but also at scientific programs. Associated member of the FAMCARE group as medical advisor. Family: Husband, children and grandchildren, son 39 years old has PWS.

SOPHIE ÇABAL-BERTHOUMIEU, CENTRE DE RÉFÉRENCE DU SYNDROME DE PRADER-WILLI AND HÔPITAL DES ENFANTS, TOULOUSE.
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ANNA-MALIKA CAMBLATS, UNIVERSITÉ DE BORDEAUX. *anna-malika.camblats@hotmail.fr*

I'm a young researcher specialized in Cognitive Psychology and Neuropsycho-logy. I have a PhD in psychology obtained at the University of Bordeaux in 2015. After visiting the University of Burgundy (2016-2017) and the University of Toulouse - Jean Jaurès (2017-2018), I came back to the University of Bordeaux in 2018 as a postdoctoral researcher. For the past 5 years, I have devoted my research to the study of the emotional functioning of adults and children with Prader-Willi Syndrome as well as its repercussions on cognition (language, attention), behavior, family and institutional environments.

SUZANNE CASSIDY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO. *suzannecassidy@comcast.net*

Dr. Cassidy is a Medical Geneticist who is a Clinical Professor of Pediatrics in the Division of Medical Genetics at the University of California, San Francisco. She specialized in Prader-Willi syndrome clinically and in her clinical research for 40 years prior to her retirement, conducting specialized clinics for PWS throughout that time. A founding member of IPWSO and IPWSO President from 2010-2016, she is currently on the IPWSO Clinical and Scientific Advisory Board. She is also on the PWSA(USA) Scientific Advisory and Clinical Advisory boards. Dr. Cassidy has been a frequent speaker about PWS at educational and medical conferences to both medical and lay audiences around the world and is widely published on the condition.

ANTONIO CRINÒ, BAMBINO GESÙ CHILDREN'S HOSPITAL, RESEARCH INSTITUTE, PALIDORO (ROME). *nino3381@gmail.com*

Dr Crinò is an Adult and Pediatric Endocrinologist and Diabetologist. Coordinator of a multidisciplinary approach to the clinical management of patients with Prader-Willi syndrome - Reference Center for PWS - Bambino Gesù Hospital, Research Institute - Palidoro (Rome), Italy (followed more than 250 PWS patients). He was Coordinator of the Genetic Obesity Study Group of the Italian Society of Pediatric Endocrinology and Diabetology (SIEDP). He is a member of the Executive Committee of the National Federation of patients with PWS. The focus of his research and clinical work is in many fields such as in rare diseases and genetic obesity, particularly in Prader-Willi syndrome (metabolic and hormonal problems, bariatric surgery etc).

Dr Crinò collaborates with the National Federation of PWS patients and the Genetic Obesity Study Group of SIEDP in the project for "Transition of PWS patients" and in the "National Registry of PWS Project" (the latter together with the National Institute of Health - Center for Rare Diseases). He has organized and participated actively in many congresses and scientific meetings regarding the Prader-Willi syndrome. His scientific activity has allowed him to produce many abstracts for National and International Congresses and more than 100 publications for international journals.

JUDE P. CRINO, UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE. *jcrino@som.umaryland.edu*

A Youngstown, Ohio, USA native, Dr. Jude Crino earned his Doctor of Medicine degree from Wright State University in Dayton, Ohio, where he also completed his residency in Obstetrics and Gynecology. Following his fellowship in Maternal-Fetal Medicine at Johns Hopkins University School of Medicine in Baltimore, Maryland, he joined the faculty of the University of Texas-Houston Medical School where he was Director of Obstetric Ultrasound in the Department of Obstetrics, Gynecology, and Reproductive Sciences before returning to Johns Hopkins as Director of Perinatal Ultrasound

in the Department of Gynecology and Obstetrics. He is currently an Associate Professor, Associate Chair, and Director of Patient Safety, Risk Mitigation, and Care Enhancement in the Department of Obstetrics, Gynecology, and Reproductive Sciences at the University of Maryland School of Medicine in Baltimore. His areas of expertise and research include obstetric ultrasound, prenatal diagnosis of fetal anomalies and syndromes, fetal therapy, high risk obstetrics, patient safety and quality improvement, and global health.

JARRON DODDS, GARVAN INSTITUTE OF MEDICAL RESEARCH AND UNIVERSITY OF NOTRE DAME. *jarron.dodds1@my.nd.edu.au*

Jarron is a member of the Prader-Willi Syndrome and Genetic Forms of Diabetes group, at the Garvan Institute of Medical Research in Sydney, Australia. He holds a Bachelor of Medical Science from the Australian National University, and in 2015 received first class honours from the University of Sydney for his thesis which investigated the effect of diet-induced weight loss on bone density and muscle strength. Jarron has just completed a post-graduate degree in Medicine and will commence his internship at St Vincent's Hospital Melbourne next year. He is keen to pursue further research and clinical experience in the field of overweight and obesity, in particular with Prader-Willi syndrome, in coming years.

DR. DAN DRISCOLL, MD, PHD, UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE, USA. *driscdj@peds.ufl.edu*

Dr. Driscoll is a Professor of Pediatrics and Genetics, as well as the Hayward Professor of Genetics Research, at the University of Florida College of Medicine. He has been conducting clinical and laboratory research on Prader-Willi syndrome since the late 1980's. He has been a major contributor to the understanding of the genetics of Prader-Willi syndrome (PWS) and genomic imprinting in the PWS region as well as to the elucidation of the natural history of PWS. His group devised the technique (DNA methylation analysis) that is used around the world to diagnose PWS.

Dr. Driscoll is widely published on PWS and a major spokesperson on PWS in the US and internationally. He has had an active PWS clinic for the last 30 years and he was the principal investigator for the PWS component of an NIH funded 12 year national Rare Disease Center grant. He has served on the PWSA (USA) Board of Directors for the last 20 years and is currently the Chair of the Clinical Advisory Board for PWSA (USA), as well as the Chair of the Clinical and Scientific Advisory Board for the International Prader-Willi Syndrome Organization (IPWSO).

URS EIHOLZER, CENTER FOR PEDIATRIC ENDOCRINOLOGY ZURICH. *urs.eiholzer@pezz.ch*

Prof. Dr. med Urs Eiholzer was trained by Prof. Andrea Prader and has been dealing with Prader-Willi syndrome ever since. He is head of the Pediatric Endocrinological Centre Zurich (PEZZ) and is author of numerous scientific publications. Some of his books on Prader Willi Syndrome are directed at families and caregivers. More than 100 PWS patients are being treated in the PEZZ.

NAWELLE FAMELART, UNIVERSITY OF TOULOUSE. *nawelle.famelart@univ-tlse2.fr*

Doctor in psychology, my research has focused on typical and atypical development of emotions in children. I conducted studies to better understand the relation between some emotional competencies in children with typical development, but also in children with a rare genetic disease. I carried out my thesis under the supervision of Pr Michèle Guidetti (CLLE UMR CNRS 5263) and Pr Maithé Tauber (PWS Reference Center, Children hospital in Toulouse). The aim of my thesis was to improve knowledge on the development of emotions in children with Prader-Willi syndrome and develop an intervention programme aimed to improve the emotional skills of these children.

Currently, I have a Temporary Lecturer and Research Assistant position at the University of Toulouse and my objective is to improve therapeutic care and quality of life for patients with emotional difficulties.

JANICE FORSTER, MD, PITTSBURGH PARTNERSHIP, USA. *janiceforstermd@aol.com*

Janice Forster, MD is a developmental neuropsychiatrist from Pittsburgh PA who has been working with children, adolescents, adults with PWS and their families for over 30 years. She has clinical experience with all levels of severity of the syndrome and across all living situations, from family to group home to inpatient hospitalization. Because she has presented across the USA and around the world, Dr Forster has a "world's-eye view" of how PWS is managed. More recently she has become involved in research exploring the developmental phenomenology of PWS and the efficacy of interventions to reduce stress in fathers of adolescents with PWS. She is "one-half" of the Pittsburgh Partnership (www.pittsburghpartnership.com), established 15 years ago with Dr Linda Gourash, for clinical consultation and education of professionals, families, and care givers. In addition to serving on the Clinical and Scientific Advisory Board of IPWSO, Dr Forster is a member of the Clinical Advisory Board of PWSA-USA.

ESTELA GARCÍA-ALCARAZ, UNIVERSITY OF OTTAWA. *egarcia@uottawa.ca*

I completed the Linguistic Communication and Multilingual Mediation PhD program at Pompeu Fabra University (Barcelona, Spain) and I am in the process of completing my second PhD in Hispanic Linguistic at the University of Ottawa (Canada). I also hold an MA in Linguistics and Technological Applications (Pompeu Fabra University) and a second MA in the Training of Teachers of Spanish as a Foreign Language (University of Barcelona). Before, I completed a double BA in Linguistics and in Translation and Interpreting (Pompeu Fabra University). My current research focuses on the study of bilingualism individuals with atypical language development, especially the case of Prader-Willi syndrome.

JUNE-ANNE GOLD, UNIVERSITY OF CALIFORNIA, IRVINE. *juneannegold@gmail.com*

Associate Professor in the Pediatrics Department in Clinical Genetics and Metabolic Genetics at Loma Linda University School of Medicine and HS Clinical Associate Professor in the Department of Pediatrics and Division of Genetics and Genomics at University California Irvine. Trained in London and Oxford in Pediatrics and genetics. She relocated to the USA in 2004.

LINDA GOURASH, MD, PITTSBURGH PARTNERSHIP, USA. *lgourash@icloud.com*

Dr Gourash is board certified as a Developmental and Behavioral Pediatrician. As the Medical Director of the Prader-Willi and Behavioral Disorders Program of the Children's Institute of Pittsburgh she worked for more than 5 years almost exclusively with children and adults with Prader-Willi Syndrome who were referred for inpatient crisis intervention from throughout the USA and Canada. Subsequently Dr Gourash has served on the Board of Directors of the Prader-Willi Syndrome Association of the USA. She is currently providing clinical consultation for the International Prader-Willi Syndrome Organization and the PWSA-USA. She provides consultation and educational programs throughout the US and internationally through Pittsburgh Partnership, Specialists in PWS. (www.pittsburghpartnership.com)

PROFESSOR TONY HOLLAND, UNIVERSITY OF CAMBRIDGE, UK. *tonyipwso@gmail.com*

Tony Holland trained in Medicine at University College and University College Hospital, London, qualifying in 1973. After some years in General Medicine he trained in Psychiatry at the Maudsley Hospital and Institute of Psychiatry in London. From 1992 to 2002 he held a University Lecturer's post in the Section of Developmental Psychiatry in the University of Cambridge, and in 2002 was awarded the Health Foundation Chair in Learning (Intellectual) Disability establishing the Cambridge Intellectual and Developmental Disabilities Research Group (www.CIDDRG.org.uk). His specific research interests include the eating, behavioural and mental health problems associated with

having Prader Willi Syndrome (PWS); the relationship between Down's syndrome and Alzheimer's disease, and also clinical/legal issues relevant to the needs of people with intellectual disabilities. With colleagues he has published research extensively on these topics in academic and practice-based journals. He works closely with charitable organisations and has been psychiatric advisor to, and Patron of, the UK PWS Association and since 2016 he has been President of IPWSO. In 2010 he was elected a Fellow of the UK Academy of Medical Sciences. In 2015 he was awarded a CBE in the Queen's Birthday Honours for services to psychiatry. Since October 2015 he has held an Emeritus position at the University of Cambridge.

AMANDA HOR, GARVAN INSTITUTE OF MEDICAL RESEARCH, ST VINCENT'S HOSPITAL AND UNIVERSITY OF NEW SOUTH WALES. *a.hor@garvan.org.au*

Amanda is an Endocrinology trainee doctor who has long held a deep interest in Endocrine medicine, in particular type 2 diabetes and obesity. Her career mission is to enhance the lives of those with obesity and diabetes through education, advocacy and innovative research. She is currently completing her PhD is on the topic of appetite, gastric emptying and safety of GLP-1 agonists in Prader-Willi syndrome at the Garvan Institute of Medical Research in Sydney Australia under the supervision of Prof Alex Viardot and Prof Lesley Campbell. She is keen to understand better the gastric emptying speed in PWS, a less researched but important area in PWS.

CHARLOTTE HÖYBYE, KAROLINSKA UNIVERSITY HOSPITAL AND KAROLINSKA INSTITUTE, SWEDEN. *charlotte.hoybye@karolinska.se*

Graduated 1986 from Medical School. Certificate as specialist in Internal Medicine 1993 and in Endocrine Diseases 1996. Since 2001 Senior Consultant in Endocrinology, from 2004 to 2017 Head of the Pituitary Section in the department. Since 2010 head of the Expert Group for Treatment of Endocrine and Metabolic Diseases, The Drug and Therapeutic Committee, Stockholm County. Member of the steering committee for the PWS-Clinical Trial Consortium and IPWSO's Clinical & Scientific Advisory Board. PhD 2003 from Karolinska Institute on the thesis "Endocrine and metabolic aspects of adult Prader-Willi syndrome with special emphasis on the effect of growth hormone treatment". Associate professor in Endocrinology, Karolinska Institute 2007.

NATHALIE KAYADJANIAN, PHD, FOUNDATION FOR PRADER-WILLI RESEARCH, USA. *nathalie.kayadjanian@fpwr.org*

Nathalie Kayadjanian, Ph.D is an expert in translational biomedical research in rare diseases with extensive R&D experience in academia, biotech, and the pharmaceutical industry in Europe and the USA. For the past twelve years, Nathalie has occupied top management positions in patient-driven non-profit research organizations as Associate Science Director of the French Association against myopathies (AFM) and Associate Director of biomedical research of the Amyotrophic Lateral Sclerosis Association (ALSA) in the US where she developed and implemented strategies to accelerate the development of innovative therapies for neurodegenerative and rare diseases.

Nathalie joined the Foundation for Prader-Willi Research (FPWR) in 2015 as the Director of Translational Research and has been instrumental in guiding and developing the FPWR 5-year strategic research plan. She is leading and developing a number of translational programs for Prader-Willi syndrome (PWS) including a Clinical Trial Network in the US and Canada; a Preclinical Animal Network to improve reproducibility and predictivity of PWS mouse models and serve as a drug screening platform; a biobank of induced pluripotent stem cells to support the development of PWS cell models and drug development. She is also the Executive Director of the PWS- Clinical Trial consortium that was launched in 2015 to address clinical trial challenges in PWS. She received her Ph.D in Neuroscience from the University Pierre and Marie Curie in Paris and did a postdoctoral training at the Salk Institute in La Jolla, USA.

VIVIAN H. LIN, MD, MILLENDO THERAPEUTICS, INC. *Lin@millendo.com*

Vivian Lin, VP of Clinical Development at Millendo Therapeutics in Ann Arbor, MI, is a general adult endocrinologist. She received her undergraduate degree in Biochemistry and Molecular Biology from Harvard University and her MD from the University of Michigan; and she completed Internal Medicine residency and Endocrinology fellowship programs at the University of Michigan. For the past 18 years, she has designed and conducted clinical trials of potential therapeutics, primarily in the cardiovascular and metabolic disease space. She has been at Millendo for nearly 4 years.

SHAWN E. MCCANDLESS, CHILDREN'S HOSPITAL COLORADO. *shawn.mccandlesschildrenscolorado.org*

Shawn E. McCandless, MD, is Professor of Pediatrics, and the Section Head for Genetics and Metabolism at the University of Colorado Anschutz Medical Campus and Children's Hospital Colorado. He is past President of the Society for Inherited Metabolic Disorders (SIMD). His research has focused on inborn errors of metabolism (IEM) and Prader-Willi syndrome (PWS), including publicly and industry funded clinical trials for children and adults with IEMs and PWS. After training with Dr. Suzanne Cassidy, he has been the Medical Director of PWS multi-disciplinary clinics in North Carolina, Ohio, and now in Colorado. He is board certified in Pediatrics (1992), Clinical Genetics (1999), and Clinical Biochemical Genetics (2005). He is a fellow of the American Academy of Pediatrics and of the American College of Medical Genetics, and he serves on the Board of Directors of the SIMD.

ESTELA MORALES PERALTA, MEDICAL UNIVERSITY OF HAVANA. *fornaris@infomed.sld.cu*

Estela Morales Peralta is a Cuban-born Clinical Geneticist, Professor at the Medical University of Havana for 36 years and, Senior Researcher. She earned her MD in 1983, first degree specialist of clinical genetics (1986), second degree specialist of Clinical Genetics (1991), PhD in 2006, through Medical University of Havana. She worked as full Professor of Genetics at the University of Asmara, Eritrea (2010-2012). Member of the staff of the Specialty of Clinical Genetics and that for Masters of Genetic Counseling and Medical Genetics. Tutor of 15 residents' thesis, 69 Master's thesis and advisor of three PhD thesis. In the last 5 years she has presented 41 papers in National and International Conferences and published 4 chapters of books, 17 scientific articles. Vice President of the Cuban Society of Human Genetics. She is a member of board for teaching ranks promotion, president of the state board examination for specialty of Clinical Genetics and of master's degrees; and secretary of the 2nd degree in Genetics examination board; associate editor, advisor and arbiter of five Scientific Journals.

JUANA MUÑOZ-LICERAS, UNIVERSITY OF OTTAWA AND UNIVERSIDAD NEBRIJA, MADRID. *Juana.Munoz-Liceras@uottawa.ca*

Juana M. Liceras is a Distinguished University Professor and a professor of Hispanic and General Linguistics in the Department of Modern Languages and the Department of Linguistics of the University of Ottawa (Ottawa, Canada), as well as the director of the Language Acquisition Research Laboratory. She is a Senior Researcher in the Applied Languages Program of the Universidad Nebrija (Madrid, Spain), one of the two editors of Languages and of the Spanish Journal of Applied Linguistics (RESLA/SJAL) as well as a member of the editorial board of several periodicals, among them Second Language Research, Journal of Spanish Language Teaching and Lengua y Migración. She is also a member of the editorial board of the John Benjamins' book series Romance Languages and Linguistic Theory and Studies in Hispanic and Lusophone Linguistics. Her research interests and publications deal with the relationship between linguistic theory and language acquisition, bilingualism in typical and non-typically developing populations, comparative grammar and language contact.

ANNA ROSENBERG, ERASMUS UNIVERSITY MEDICAL CENTER. *a.rosenberg@erasmusmc.nl*

My name is Anna Rosenberg and I am a master student at the Erasmus Medical Center in Rotterdam, the Netherlands. After I finished my Bachelor of Medicine, I started a Research Master Clinical Research at the Netherlands Institute for Health Sciences (NIHES), which I will finish within a year. I am currently investigating the health problems occurring in adults with Prader-Willi syndrome, RASopathies, Williams-Beuren syndrome, CHARGE syndrome and Klinefelter syndrome. After I finish my Research Master, I will continue this research as a PhD-student.

DANIELA RUBIN, PHD, CALIFORNIA STATE UNIVERSITY,FULLERTON, USA. *drubin@fullerton.edu*

Dr Daniela A. Rubin is physical education teacher native of Argentina. In 1999 she moved to the Unites States to purse her graduate studies in the field of exercise physiology at the University of North Carolina Chapel Hill. She is a Professor in the Department of Kinesiology at California State University Fullerton. Her interest in the topic of exercise endocrinology, inflammation and obesity led to several projects comparing hormonal, metabolic, and inflammatory responses to exercise in children, including youth with Prader-Willi Syndrome (PWS). As she became more involved in understanding the challenges faced by people with PWS, her studies sought to examine exercise aspects in this syndrome from a multidimensional perspective. Her studies characterized physical activity patters using accelerometry, examined motor aspects in terms of sensory reception and integration and motor proficiency, cardiorespiratory responses to exercise, energy expenditure, body composition and phenotype. Her team also developed and tested a 24 weeks physical activity intervention in 116 children with and without PWS (Active Play at Home©, FunDoRoo©). Using a game-based approach parents completed an at-home routine with their children showing improvements in motor proficiency, health-related quality of life and inflammatory and metabolic factors. Her last intervention study involved children ages 4-7 doing physical activity with their parents. She has served as a board member in the Prader-Willi California Foundation since 2013.

PARISA SALEHI, SEATTLE CHILDREN'S HOSPITAL, UNIVERSITY OF WASHINGTON.
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Dr. Parisa Salehi is an Associate Professor of Pediatrics at the University of Washington in the Division of Endocrinology at Seattle Children's Hospital in Seattle, WA, USA. Her medical training was done at the University of Nevada School of Medicine. Her pediatric training was at the Children's Hospital of Orange County and subsequent pediatric endocrine training was at the Children's Hospital of Los Angeles. She has been doing research related to Prader-Willi Syndrome since her fellowship training in 2010. She is currently the clinical director of the Prader-Willi Syndrome clinic at Seattle Children's Hospital, an interdisciplinary clinic started in 2014 which is involved in clinical care and research related to children and adolescents with PWS.

ANN O. SCHEIMANN, M.D., M.B.A, JOHNS HOPKINS HOSPITAL. *ascheima@jhmi.edu*

Dr. Scheimann received her doctorate of medicine at the University of Cincinnati School of Medicine and completed her pediatric residency and pediatric gastroenterology and nutrition fellowship at Baylor College of Medicine/Texas Children's Hospital. She was full time faculty within the Division of Pediatric Gastroenterology and Nutrition at Baylor College of Medicine until 2000 when she moved to join the full-time faculty within the Department of Pediatrics/Division of Pediatric Gastroenterology at Johns Hopkins School of Medicine but remained adjunct faculty at Baylor College of Medicine directing the Prader-Willi Syndrome Clinic at Texas Children's Hospital. Dr. Scheimann completed a Masters in Health Sciences Management at Johns Hopkins School of Business in 2005. Dr. Scheimann's focus of research interest has been in nutrition and obesity with special areas of interest in Prader-Willi Syndrome and nonalcoholic fatty liver disease. She has authored or co-authored to date approximately 60 peer-reviewed publications in addition to book chapters, and meeting presentations.

DIANE STAFFORD, STANFORD UNIVERSITY. *dejs@stanford.edu*

Dr. Diane Stafford is a Clinical Professor of Pediatric Endocrinology at Stanford University Medical School and Lucile Packard Children's Hospital. She completed her pediatric residency at Stanford and her endocrinology training at Boston Children's Hospital where she then practiced for 20 years. Both in Boston and at Stanford, Dr. Stafford specializes in the endocrine sequelae of Prader Willi syndrome, providing both hormonal management and coordination of care for children with PWS.

MAÏTHÉ TAUBER, PEDIATRICIAN AND PROFESSOR OF PEDIATRICS, HÔPITAL DES ENFANTS AND PAUL SABATIER UNIVERSITÉ, TOULOUSE, FRANCE. *tauber.mt@chu-toulouse.fr*

Position held:

1. Coordinator of the French Reference Centre for Prader-Willi Syndrome and other rare disorders with obesity and/or feeding disorders
2. Head of the endocrinology, obesity, bone diseases, genetics and medical gynecology team
3. President of the regional network for pediatric obesity and of the national association for the networks on pediatric obesity

Active research interests particularly those relevant to PWS:

1. 25 years of experience in the care of PWS children with particular emphasis on early diagnosis, endocrine issues, treatment of comorbidities, multidisciplinary care, new treatments for PWS.
2. Research on obesity particularly in prevention, organization of the regional network for pediatric obesity, epidemiological studies and genetic studies in collaboration
3. Research on ghrelin and oxytocin.

DÓRA TÖRÖK MD, PHD, ASSOCIATE PROFESSOR OF PEDIATRICS AT SEMMELWEIS UNIVERSITY, BUDAPEST, HUNGARYÇ. *torokdora@gmail.com*

Dr. Török is associate professor of pediatrics at Semmelweis University, Budapest, Hungary. She received an MD in 2000 at Semmelweis University, Budapest, and a PhD in pediatric endocrinology in 2005 (Semmelweis University, Budapest). She performed postdoctoral research works in Vienna (Allgemeines Krankenhaus, Wien, Austria) and in The Hospital for Sick Children (Toronto, Canada). She gained specialist certification in pediatrics and endocrinology. Her clinical practice covers a wide range of pediatric endocrinology. Her main research interests are Prader-Willi syndrome, insulin resistance, congenital adrenal hyperplasia and endocrine tumors. She is the happy mother of two children.

HAROLD VAN BOSSE, SHRINERS HOSPITAL FOR CHILDREN, USA. *HvanBosse@Shrinenet.org*

Harold J.P. van Bosse, M.D. has been practicing pediatric orthopaedic surgery exclusively since completing his orthopaedic residency at the University of Illinois in Chicago in 1994, and his fellowship at Toronto's Hospital for Sick Children in 1995. He joined the staff of the Philadelphia's Shriners Hospital for Children in 2008, allowing for a more focused practice treating conditions of special interest. His interest in Prader-Willi syndrome developed from treating a 2 year old child with PWS and severe scoliosis. Through that patient, Dr. van Bosse was introduced to the community of specialists caring for children with PWS, joining them to round out the comprehensive care of these challenging and rewarding patients. Much of his efforts have been treating the very young child with PWS and spine deformities. For these children, treatment devoted to the least invasive modalities that will preserve spinal growth and chest development. These include bracing, spinal casting and expandable implants, to avoid a spinal fusion during childhood. Dr. van Bosse is a member of the Clinical and Scientific Advisory Board of IPWSO, the Clinical Advisory Board of PWSA-USA, and has given talks on the orthopaedics of PWS at PWSA-USA, FPWR, PWANY and PWCF meetings over the years.

KATE WOODCOCK, UNIVERSITY OF BIRMINGHAM, UK. *K.A.Woodcock@bham.ac.uk*

Dr Kate Anne Woodcock is a Senior Lecturer at the Centre for Applied Psychology in the School of Psychology at the University of Birmingham, UK. Her research focuses on young people who face psychological and behavioural difficulties, often those linked to neurodevelopmental disorder. Several lines of her research focus specifically on individuals with Prader-Willi syndrome. Kate's work has examined factors that come together to precipitate behaviours that can be challenging for individuals with Prader-Willi syndrome, such as temper outbursts. Her team is currently engaged in work that applies this knowledge to the development of intervention strategies. For example, caregiver led behavioural support strategies, cognitive training intervention programmes, and early intervention strategies. Kate carried out her PhD research at the University of Birmingham between 2005 and 2008. Two years of her Postdoctoral Research were at Peking University, China between 2011 and 2013. Kate held a lectureship position at the School of Psychology, Queen's University Belfast between 2014 and August 2017.

KENICHI YAMADA, UNIVERSITY OF NIIGATA. *yamadak@bri.niigata-u.ac.jp*

Kenichi Yamada, MD, PhD, is an associate professor. His research interests include clinical application of magnetic resonance imaging technology to elucidate the pathophysiology of the brain in pediatric neurodevelopmental disorders, based on his clinical experiences as a physician in child neurology, developmental medicine, and behavioral pediatrics.

CLINICAL AND SCIENTIFIC CONFERENCE: SPEAKER ABSTRACTS

I. GENETICS, EPIGENETICS & ANIMAL MODELS

I-1. INVITED TALK: "GENETICS IN PWS: WHERE WE HAVE BEEN AND WHERE WE ARE GOING"

▸ **Daniel J. Driscoll**
Department of Pediatrics and Center for Epigenetics, University of Florida College of Medicine, Gainesville, FL, USA
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Prader-Willi syndrome (PWS) is a complex contiguous gene syndrome involving multiple imprinted loci within chromosomal region 15q11.2-q13. Loss of the paternally expressed SNORD116 locus is a major contributor to the phenotype, but multiple other genes within the region that are only paternally expressed also contribute to the phenotype.

There are 3 main genetic mechanisms (molecular classes) for PWS: paternal deletion, maternal uniparental disomy (UPD) 15, and imprinting defect. Within each molecular class there are subclasses. Approximately 90% of the deletion class can be accounted for by type 1 and 2 deletions, but 10% are atypically sized deletions which can impact the phenotype.

DNA methylation analysis can diagnose >99% of all cases of PWS, but it cannot determine the molecular class. Therefore, it is a powerful screening tool for PWS, but once the diagnosis of PWS is established the molecular class needs to be determined for genotype-phenotype correlation and genetic counselling purposes. DNA methylation is also available for prenatal diagnosis and for newborn screening. Mosaic imprinting defects and mosaic trisomy 15 with maternal UPD 15 are underdiagnosed conditions.

The exact role and targets of the PWS imprinted genes is an area of active research. Also, the role of the upstream exons of the SNURF-SNRPN locus is currently not clear. Some genes elsewhere in the genome are emerging as targets of the PWS imprinted loci and will be discussed. Gene therapy may have a role to play in the treatment of PWS in the future.

I-2. INVITED TALK: "AN UPDATE ON MOUSE MODELS OF PWS", TALK THE ZAFGEN LECTURE

▸ **Jim Resnick**
Department of Molecular Genetics and Microbiology, University of Florida, Gainesville, FL
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Over 25 spontaneous and targeted mutations affecting imprinted genes at the orthologous mouse PWS locus have been reported. This long list includes mutations that target individual PWS genes, as well as large deletions and imprinting center mutations that inactivate multiple PWS genes. These mutants have provided important insights into the inheritance and pathogenesis of PWS. Although many PWS traits have been modeled by existing mice, to date no single mouse model recapitulates all traits commonly seen in individuals with PWS. The presentation will highlight select mouse models that replicate salient PWS traits, as well as traits that have not been well replicated in mice. With a few notable exceptions, PWS mice have had limited use as preclinical models with which to assess the efficacy of new therapeutics. Such studies have been hindered by insufficient phenotypic characterization, heterogenous assessment methods, and inadequate knowledge of the translatability of human phenotypes into animal read-outs. An initiative by the PWS mouse models community to address these preclinical needs will also be described.

II. ENDOCRINOLOGY

II-1. INVITED TALK: "OXYTOCIN IN PRADER-WILLI SYNDROME"

▸ Maithé Tauber
Centre de Référence du syndrome de Prader-Willi, Hôpital des Enfants, Toulouse, France, 6INSERM U1043, Centre de Physiopathologie de Toulouse Purpan, Université Paul Sabatier, Toulouse, France
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Oxytocin (OXT) is a neuropeptide that plays an important role in modulating social interactions and mother-infant bonding. Quantitative neuroanatomical studies of postmortem human hypothalamic tissue from patients with Prader–Willi Syndrome (PWS) have demonstrated a reduced number and volume of OXT neurons in the paraventricular nucleus in comparison with controls. Similarly, an alteration in the OXT system was described in PWS mouse models. In patients with PWS increased levels on circulating levels have been documented. After the first study we published in 2011 using OXT in adults with PWS1 several clinical trials have been implemented administering OXT in children, adolescents and adults with PWS2,3,4. All but one study reported positive effects on behavior albeit the effect on eating behavior is poor and the main effect of OXT remained to be defined. Only one study showed negative results in adolescents and adults with a worsening of temper tantrums particularly with high doses of treatment. Additional clinical trials are ongoing in children and adolescents.

One proof of concept study was performed in infants with PWS showing positive effects on oral and social skills5 therefore recapitulating the effects observed in the mice model with MAGEL2 deficit. Therefore, OXT in this period of life may be of unique interest by improving the first nutritional phase including increasing appetite and oral motor skills decreasing social withdrawal and improving mother-infant interactions. Most importantly is the change of connectivity of the orbitofrontal cortex observed in brain fMRI after OXT treatment in infants with PWS. Neurons of this brain region is known to be involved in feeding regulation and social stimuli-responsive neurons. This is online with the correlations observed between brain changes and changes on oral and social skills. Long term effect of OXT treatment after 3-4 years documented the good tolerance of an early short course of oxytocin and in communicating skills. It remains to document the effect vs placebo, to find the best dose and duration of the treatment before using it in routine in neonates and infants. That will be done in a further international clinical trial which will start soon. Moreover, OXT may have a role in brain plasticity early in life but seems to also display a physiological role and may be useful afterwards.

Interestingly induced pluripotent stem (iPS) cells differentiated into neurons are useful tools to understand the effect of OXT in neurons. Indeed, it has been possible to show impaired prohormone processing in these neurons driving OXT deficit6.

In addition, OXT and ghrelin both impaired in PWS are functionally linked. Indeed, administration of OXT modifies circulating ghrelin levels in infants. OXT and ghrelin G protein coupled receptors may form heterodimers that modify the effect of OXT7. Both OXT and ghrelin play a role in controlling appetite and behavior and both hormones are used in ongoing clinical trials in PWS. Therefore, the challenge will be to identify the specific and possibly complementary role of these two hormones and their use in PWS.

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II-2. INVITED TALK: "AN OVERVIEW OF ENDOCRINOLOGY IN ADULTS WITH PWS",THE LEVO THERAPEUTICS LECTURE

▸ Charlotte Höybye
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Introduction: Many symptoms in Prader-Willi syndrome (PWS) are similar to symptoms caused by insufficient hormone levels. In this presentation symptoms and treatment of growth hormone deficiency, central adrenal insufficiency, central hypothyroidism and hypogonadism in adolescents and adults with PWS will be discussed.

Muscular hypotonia, abnormal body composition and low energy expenditure are well-known symptoms of growth hormone deficiency (GHD). Available knowledge suggests some degree of GHD in adults with PWS and studies have consistently shown significant benefits of GH therapy on body composition, physical and psycho-social function in adults with PWS. GH might increase the risk for type 2 diabetes, and glucose levels should be monitored during GH treatment. Adrenal insufficiency is characterised by fatigue, weight loss and insufficient response to stress and central adrenal insufficiency was hypothesized to be responsible for sudden deaths in PWS. However, most studies indicate that hypocortisolism is rare, and evaluation and treatment only necessary when clinically indicated.

Increase in weight, lethargy and low body temperature are characteristics of hypothyroidism. Central hypothyroidism has been reported with a high frequency in children but not in adults. Due to similarities with symptoms in PWS regular follow-up of thyroid function is recommended.

Sex hormones are important for appearance of body gender, body composition, bone mineral density, fertility and quality of life. Primary hypogonadism is most frequent in PWS but there is a continuum from complete primary hypogonadism to complete central hypogonadism. There is no consensus on management of hypogonadism in PWS and an individual consideration of benefits and risks with sex-hormone treatment is recommended. Inhibin-B, a marker of fertility, is undetectable in most adults with PWS. Five pregnancies have been described in PWS women. Fertility in PWS males has not been reported.

Conclusions: Some symptoms in adults with PWS share similarities with hormone insufficiencies. As some of the hormone insufficiencies are common, diagnosis and hormone replacements are important along with prevention of obesity and treatment of comorbidities for optimal care in adults with PWS.

II-3. "CENTRAL ADRENAL INSUFFICIENCY IS RARE IN ADULTS WITH PRADER-WILLI SYNDROME"

▸ Anna Rosenberg[1], Karlijn Pellikaan[1], Kirsten Davidse[1], Christine Poitou Bernert[2,12,14], Charlotte Höybye[3,12,14], Graziano Grugni[4,12,14], Tania Markovic[5,12], Antonino Crinò[6,12], Anthony Goldstone[7,12], Assumpta Caixàs[8,12], Muriel Coupaye[2], Sjoerd van den Berg[9], Stephany Donze[10], Anita Hokken-Koelega[10,11,13,14], Aart Jan van der Lely[1,14], Laura de Graaff1,[12,13,14]

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Introduction: Prader-Willi syndrome (PWS) is associated with deficiencies of several hypothalamic-pituitary hormones. Central adrenal insufficiency (CAI) has been reported in PWS with prevalences ranging from 0% to 60%, depending on endocrine testing methods, cut-off values and population studied (pediatric vs adult). It has been speculated that CAI might be responsible, at least in part, for the high mortality (3% a year across all ages) in patients with PWS. If CAI is present, timely diagnosis and treatment is needed to prevent avoidable mortality. There are no guidelines on the appropriate evaluation and management of CAI in adults with PWS. Many patients with PWS receive standard hydrocortisone (HC) treatment around periods of physical and/or psychological stress. As the behavioural phenotype of PWS includes temper outbursts, this may lead to frequent HC administration by caregivers, at least in adults. Frequent administration of HC increases the risk of obesity, hypertension, osteoporosis and diabetes, already major problems in adults with PWS. It is therefore of utmost importance to assess the real prevalence of CAI in order to prevent both under- and overtreatment with HC.

Methods: The hypothalamic-pituitary-adrenal axis was tested in 71 adult subjects (55 Dutch, 10 French, 6 Swedish) with genetically confirmed PWS. Multiple dose metyrapone (MTP) test was performed in 45 subjects and insulin tolerance test (ITT) in 26 subjects. When levels of 11-deoxycortisol (S) during MTP were greater than 230 nmol/L (7.6 g/dL) or levels of cortisol during ITT were greater than 500 nmol/L (18.1 kg/dL), adrenal insufficiency was excluded. Additionally, we collected medical files of 630 adult patients with PWS from Italy (240), France (110), the Netherlands (106), Australia (60), Spain (45), Sweden (38) and the United Kingdom (31), which we recognize may not represent the entire PWS population. We reviewed these files for data on previous surgery and/or health problems related to hypocortisolism.

Results: Data on 71 adult subjects (41 males and 30 females), median age (range) 26.3 yr (18.0 – 55.5), median BMI (range) 28.7 kg/m2 (20.0 – 58.2), with genetically confirmed PWS were collected. 31 subjects (44%) were using GH treatment since childhood. At MTP test, all 45 subjects had S ≥ 230 nmol/L. At ITT, all subjects had cortisol levels ≥ 500 nmol/L, apart from one subject who had a peak cortisol level of 494 nmol/L. Although this is still within measurement error for the cortisol assay, this patient was prescribed HC for use during physical stress. Even patients with a low baseline cortisol level (lowest: 102.0 nmol/L) had normal MTP or ITT test results. Both tests were tolerated well by all individuals. None of the 630 patients who had undergone surgery or infections without peri-operative or illness-associated HC treatment developed hypocortisolism.

Conclusions: CAI is rare (1.4%) in adults with Prader-Willi syndrome. Because of the low probability for CAI we recommend dynamic testing for hypocortisolism only when clinically indicated. Routine prescription of HC stress medication is not necessary.

II-4. "SYSTEMIC INFLAMMATION AND THE EFFECT OF A GLP-1 RECEPTOR AGONIST IN ADULTS WITH PRADER-WILLI SYNDROME"

▸ Jarron Dodds[1, 4], Amanda Hor[1, 2, 3], Louise Purtell[1], Lesley Campbell[1, 2, 3] & Alexander Viardot[1, 2, 3]

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Introduction: Prader - Willi syndrome (PWS) is one of the most common known genetic obesity disorders, and is associated with a reduced life expectancy due to cardiovascular disease. Increased systemic low-grade inflammation is postulated as a contributor, despite reported lower visceral fat mass and increased insulin sensitivity in PWS. In non-syndromic obesity, GLP-1 receptor agonist therapy is thought to decrease cardiovascular morbidity and mortality by reducing low grade inflammation; however, its effects have not been studied in PWS. This project aimed to assess immune cell activation markers and circulating cytokine profile, fasting and postprandially, in PWS compared to lean and adiposity-matched obese subjects. Further, to determine the acute effect of a GLP-1 receptor agonist on immune cell activation and circulating inflammatory cytokines in PWS.

Methods: Baseline and postprandial levels of immune cell activation markers were quantified via flow cytometry, and inflammatory cytokine levels measured via ELISA in 9 PWS adults and compared with 11 adiposity-matched obese and 10 healthy lean subjects. In a single-blinded, crossover design, PWS and obese subjects received either a single dose of 10 mcg exenatide (Byetta) or normal saline subcutaneously 15 minutes before consuming a standardised 600 kCal meal.

Results: PWS subjects demonstrated increased fasting and postprandial innate immune cell activation, with significantly higher expression of granulocyte and monocyte cell markers. A single dose of exenatide with a meal yielded significant decreases in innate immune cell activation markers in PWS and obese subjects. Circulating cytokines E-selectin, MIC-1 and PAI-1 were elevated in PWS compared to lean but not different to obese. sICAM-1

levels were not different between the groups. IL-6 was higher in PWS than in Obese and Lean. A single dose GLP-1 receptor agonist did not significantly lower IL-6 response postprandially.

Conclusions: We found evidence for low grade systemic inflammation in PWS, with elevated expression of innate immune cell activation markers and serum IL-6 levels. The increased IL-6 levels fasting and post-prandially appears to be specific to PWS and merits further investigation regarding its possible contribution to the cardiovascular risk. A single dose GLP-1 receptor agonist appeared effective in reducing postprandial immune cell activation, but without IL-6 suppression. Currently running investigations will examine the long-term effects of GLP-1 receptor agonists on systemic inflammation in PWS.

III. GASTROINTESTINAL & NUTRITION

III-1. INVITED TALK: "COMPREHENSIVE OVERVIEW OF DIGESTIVE ISSUES IN PRADER-WILLI SYNDROME"

▸ **Ann O. Scheimann, M.D., M.B.A**
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Nutrition and digestive issues are commonly encountered in the management of Prader-Willi syndrome with impacts upon the lifespan. This presentation will involve a summary of existing published literature relevant to digestive related issues in Prader-Willi syndrome including data from clinical practice and research studies performed on gastrointestinal emptying/motility, impact of dietary interventions upon behavior, impact of GI issues upon morbidity/mortality in Prader-Willi syndrome and preliminary data from gut microbiome analyses in Prader-Willi syndrome.

III-2. "REVIEW OF SHORT AND LONG-TERM OUTCOMES OF BARIATRIC PROCEDURES IN PRADER-WILLI SYNDROME AND OTHER HYPERPHAGIC DISORDERS"

▸ **Ann Scheimann MD MBA**
Collaborators: **Merlin Butler MD PhD, Dan Driscoll MD PhD, Janice Forester MD, Linda Gourash MD, Jennifer Miller MD**
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Introduction: Morbid obesity is an increasing concern throughout the developed and developing world with rising prevalence and anticipated significant utilization of healthcare resources over the next several decades. As there has been suboptimal results from lifestyle interventions and pharmacologic approaches to date, bariatric surgical and endoscopic procedures have increased over the past 2 decades including adolescents and children with significant post-operative improvement in weight related co-morbidities. As weight management strategies are most challenging among those with hyperphagic disorders, we chose to review published outcomes of bariatric procedures among individuals with hyperphagic genetic and acquired disorders including Prader-Willi syndrome (PWS), Melanocortin-4-Receptor Mutations (MC4R), Bardet-Biedl syndrome (BBS) and Hypothalamic Obesity (HO).

Methods: Review of existing published literature using the following search terms: Prader-Willi syndrome, Bardet-Biedl syndrome, hyperphagia, bariatric surgery, MC4R/melanocortin-4-receptor mutations, hypothalamic obesity, bariatric procedure. Information collected included demographics, genetic testing (if available), anthropometry, type of procedure, long-term outcomes and complications. Given the rarity of the disorders, case series and clinical reports were included in the analyses. Publications were carefully reviewed to minimize duplicity of data. Post-surgical outcomes were compared with outcomes of other large bariatric cohorts (e.g. LABS, Teen-LABS). T-test, Mann-Whitney, Chi-Square and Fisher's Exact Test were used for data analyses (Graph Pad Prism ® version 6.05).

Results: A total of 49 publications were identified (32-PWS, 8-MC4R, 5-BBS, 4-HO). A total of 163 adults and children with history of bariatric procedures were described with variable duration of follow-up. Procedures performed included jejunoileal bypass, gastric bypass, vertical band gastroplasty, adjustable gastric band, bilioenteric balloon (BIB), biliopancreatic diversion and sleeve gastrectomy. 117 (72%) patients with PWS, 31 (19%) patients with MC4R mutations, 7 (4%) with BBS, 8 (4%) with HO. Mean ages for procedures: HO 18.25 years, BBS 30.2 +/-9.6 years, MC4R 29.4 +/-14.6 years, PWS 19.4 +/-6 years. Variable improvement in weight- related co-morbidities was reported (PWS sleeve data: OSA resolved in 21/24 PWS vs teen sleeve patients (p=0.053), similar improvement in hypertension (p=0.68) and dyslipidemia (p=0.76 vs Teen LABS sleeve patients). There were higher rates of weight regain among patients with PWS with history of biliopancreatic diversion (p=0.01), and gastric bypass (p<0.0001) in comparison to other obese patient cohorts. Among patients with MC4R mutations, there appear to be higher rates of long- term weight regain among patients with homozygous mutations in comparison to those with heterozygous mutations in the MC4R receptor. Complications included weight regain requiring reoperation/revision, infections, adhesions/band slippage, nutritional issues (osteopenia, anemia) complications, including some deaths due to infection or gastric perforation with higher rates of complications associated with some procedures including BIB (p<0.001).

Conclusion: Bariatric procedures have been reported among individuals with hyperphagic disorders including Prader-Wlli syndrome with varying results and higher incidence of complications. Completion of genetic testing prior to completion of bariatric procedures among those with symptoms of hyperphagia should be considered as part of preoperative evaluation. Comprehensive long-term (5 years, 10 years) outcomes data including quality of life data after bariatric procedures is needed.

III-3. "LONG-ACTING GLP-1 AGONIST TREATMENT IN PRADER-WILLI SYNDROME: BENEFITS ON APPETITE, BEHAVIOUR AND COGNITION VERSUS RISKS?"

▸ **Amanda Hor[1,2,3], Renee Richens[1], Krisztina Toth[1], Saesha D'Silva[3], Jarron Dodds1, Georgina Loughnan[4], Tania Markovic[4], Lesley Campbell[1,3,2], Alexander Viardot[1,3,2]**
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Introduction: Management of hyperphagia and behavioural problems in Prader-Willi Syndrome (PWS) remains a major challenge. GLP-1 agonists have gained traction in the treatment of diabetes in people with PWS and have potential beneficial effects on the gut and brain. However, little is known yet about the safety of this drug class in people with PWS as they can delay gastric emptying (GE). Assurance on safety is paramount to avoid potentially increasing the risk of gastric necrosis. Although still controversial, previous studies have suggested that subjects with PWS may have delayed GE. To address this, we determined GE in people with PWS compared to controls by gastric scintigraphy, the most reliable, validated method. We also assessed the gastrointestinal safety of this novel drug, which has the potential to improve appetite, behaviour and cognition in those with PWS.

Methods: In this prospective interventional study (ENGAGE PWS), GE was compared in people with PWS to lean and BMI-matched obese control individuals. All subjects had a Dual Energy X-ray

Absorptiometry scan to assess body composition. Subjects with PWS who had normal GE rates were then treated with once-weekly exenatide for 12 weeks. GE was measured by gastric scintigraphy at baseline, 4 and 12 weeks, with the ingestion of 99mTc-labelled breakfast, regular blood samples and appetite assessments. For safety, treatment was discontinued in subjects with delayed GE at the 4 week assessment. All those with PWS completed the cognitive function assessment using the Cambridge Neuropsychological Test Automated Battery (CANTAB) and their parents/guardians completed a Hyperphagia Questionnaire (HQ) during their visits.

Results: 11 lean, 9 obese and 13 PWS aged 18-51yr were recruited. At the baseline visit, the average GE rate was similar in those with PWS compared to lean and obese controls, but we identified 3 subjects with PWS who had delayed GE and were thus excluded from the interventional study. Subjects with PWS who received weekly exenatide for 12 weeks showed a trend towards a mild delay in gastric emptying compared to baseline. Importantly, GLP-1 RA treatment had to be discontinued in 2 subjects at the 4 week visit due to delayed GE above the safety threshold. Fullness rating increased from baseline to week 4 while hunger ratings were unchanged. Weight, hyperphagia scores and cognition testing were variably affected by treatment.

Conclusions: Although we did not see an intrinsic delay in GE in most of the subjects with PWS, a proportion of subjects had significantly delayed GE and are not suitable for GLP-1 RA treatment. During treatment, we observed a mild delay in GE in most subjects, but importantly, greater effects on GE were seen in a small subset of patients. GLP-1 was well tolerated with beneficial effects on some of the subjects' weight and appetite. We recommend GE assessment before and/or during GLP-1 RA treatment for optimal safety.

III-4. "EFFECT OF MACRONUTRIENT COMPOSITION ON POSTPRANDIAL METABOLISM IN CHILDREN WITH PRADER-WILLI SYNDROME (PWS): PRELIMINARY FINDINGS"

▸ Maha Alsaif[1], Sarah A Elliott[2], Mohammadreza Pakseresht[1], Michelle L Mackenzie[2], Carla M Prado[1] Catherine J. Field[1] and Andrea M Haqq[1,2]

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Introduction: Meals of similar caloric content but differing in macronutrient composition may impact diet-induced thermogenesis (DIT), potentially influencing total energy expenditure (TEE). Energy expended through digestion, absorption and storage of dietary protein is higher than for carbohydrate and fat. Therefore, a high-protein (HP) diet could have an influence on energy metabolism and weight control. The aim of this study was to compare the impact of a HP diet versus a typical North American, high-carbohydrate diet (standard diet) on DIT and substrate oxidation in children with Prader-Willi syndrome (PWS). Prader-Willi syndrome is a unique clinical model of childhood obesity associated with hypotonia, hyperphagia and lower metabolic rate compared to children without PWS.

Methods: Participants completed three separate study visits separated by a two to four-week washout period. Anthropometric measurements were completed at each study visit. In a randomized, crossover study design participants were randomly allocated to two isocaloric arms: a) standard diet: 55% carbohydrate, 15% protein, and 30% fat; b) HP diet: 20% of carbohydrate, 50% protein, and 30% fat. Participants received the prescribed diets (three meals plus two snacks per day accompanied by either a powder supplement (high-protein diet) or an extra snack (standard-diet) for one day prior to each study visit and a breakfast meal inside a whole-body calorimetry unit (WBCU). Diets were designed to ensure participants were in energy balance. Resting metabolic rate (RMR), DIT and respiratory exchange ratio (RER) were assessed. Differences between diets were assessed by paired sample T-test considering a significance value of $p<0.05$.

Results: Five individuals with PWS (4F/1M, age: 14.5 ± 4.0 (11-20 years) BMI percentile: 86.2 ± 10.5 (70.2.-98.3)) were assessed. No differences were observed in the RMR (1625.5 ± 188.4 vs 1511.5 ± 168 kcal; $p = 0.49$) and DIT (200 ± 189 vs 184.3 ± 189 kcal; $p = 0.74$) measurements between HP and standard diets. However, a lower RER was observed in the HP diet in comparison to the standard diet (0.80 ± 0.2 vs 0.86 ± 0.2; $p < 0.009$).

Conclusion: Respiratory exchange ratio was lower in the HP diet compared to the standard diet in individuals with PWS; suggesting a shift towards fat rather than carbohydrate as a fuel source. Although no differences were observed in the DIT measurements between HP and standard diets, the small sample size does not allow for meaningful statistical considerations due to the high variation among groups. This preliminary data suggests a diet higher in protein may provide a metabolic advantage compared to a typical North American, high-carbohydrate diet. Future analysis of healthy children matched for age, sex and BMI percentile will confirm if individuals with PWS metabolize food differently as compared to healthy children.

III-5. "RELATIONSHIP BETWEEN ANGIOPOIETIN-LIKE LEVELS AND NON-ALCOHOLIC FATTY LIVER DISEASE IN CHILDREN WITH PRADER-WILLI SYNDROME"

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Background: A recently identified liver protein, Angiopoietin-like8 (ANGPTL8), was described to be involved in different metabolic pathways related to gluco-lipid metabolism and associated with liver function and non-alcoholic fatty liver disease (NAFLD) in adult patients with Prader-Willi syndrome (PWS). This study aimed to investigate ANGPTL8 levels in children with PWS and their controls in relation with metabolic homeostasis and NAFLD.

Subjects and Methods: 29 children with genetically confirmed PWS (M/F=17/12, age 11.4±3.1y, BMI-SDS 2.4±1.2) and 29 BMI- and age-matched controls (M/F=10/19, age 12.9±3.1y, BMI-SDS 2.7±0.4) underwent analysis of serum ANGPTL8, leptin, adiponectin, glucose homeostasis, lipid profile and liver function. Fat-free mass (FFM, kg) and fat mass (%FM) were assessed by DXA, NAFLD severity by liver ultrasonography [Shannon A, J Pediatr Gastroenterol Nutr 2011].

Results: PWS subjects showed lower FFM (30.2±9.9 vs 39.4±13.5 kg, $p<0.05$) and similar %FM (45.2±6.9 vs 43.5±6.1%, ns) but healthier glucose and lipid homeostasis than controls. Adiponectin levels were higher in PWS than controls (16.2±7.8 vs 9.4±4.4 µg/mL, $p<0.0001$), whereas ANGPTL8 (0.50±0.29 vs 0.46±0.20 ng/mL, ns) and leptin levels (30.6±18.5 vs 30.7±15.8 ng/mL, ns), prevalence of NAFLD (55.2 vs 69.0%, ns) as well as liver function profile were similar between groups. In PWS group, ANGPTL8 levels were positively associated with BMI-SDS ($p<0.05$), HOMA-IR ($p<0.01$), leptin levels ($p=0.001$) and the presence of NAFLD ($p<0.05$),

whereas in the control group they were negatively correlated with BMI-SDS ($p<0.05$). By stepwise multivariable regression analysis on the whole dataset, ANGPTL8 levels were independently predicted by BMI-SDS ($p<0.01$), leptin levels ($p<0.01$) and NAFLD ($p<0.05$).

Conclusions: Children with PWS show an healthier glucose homeostasis compared to controls. Although ANGPTL8 levels were similar between PWS and controls, our results highlight its potential role a new biomarker of insulin resistance, liver function and NAFLD in PWS children.

IV. GENERAL MEDICAL ISSUES

IV-1. INVITED TALK: "OVERVIEW AND EVALUATION: INFANTS, CHILDREN, ADOLESCENTS AND ADULTS WITH PWS"

▸ Susanne Blichfeldt MD
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Introduction: During the last 2 years the CSAB has published on the IPWSO web site Overviews and Evaluation Guidance concerning Infants, Children, Adolescents and Adults. All to be downloaded: www.IPWSO.com/medical-professionals.

Background: Medical contact and services for persons with PWS varies a lot among countries, and also inside many countries. As PWS is a very complex disease, we find it important that all have regular medical evaluations, frequency depending on individual needs, for the youngest most often, older children and adults at least yearly. If not possible at a medical center with experience in PWS, it is of value that the local physicians, having not met PWS before, have access to overviews and recommendations for evaluations, that are up to date and easy to read. Families and caregivers can read and print the recommendations, and bring it with them at medical visits.

Methods: The forms are made for the mentioned four age groups, as symptoms and needs vary and change from infancy to adulthood. The overviews describe the most often met symptoms in the actual age group, and in the evaluation guidance clinical evaluation, investigations, blood tests recommended are listed. We are aware that possibilities for investigations and treatments vary from country to country and also within countries. Costs and economical support for medical services vary, but many of the recommendations especially concerning clinical evaluations and guidelines can be followed in most countries. The plan is to review the text on a regular basis, and change and add information according to the newest knowledge. Examples from the publications will be presented

Conclusion: The CSAB hope the Overviews and Evaluation guidance published can be used and found useful for both families, caregivers and medical professionals. We look forward to receiving feedback for continuing updating and bettering of the publications.

IV-2. INVITED TALK: "MEDICAL CARE FOR PATIENTS WITH PWS AT THE NATIONAL NETWORK OF MEDICAL GENETIC SERVICES IN CUBA"

▸ Estela Morales Peralta, Anitery Travieso Tellez, Yudelkis Benitez Cordero, Teresa Collazo Mesa, Luis Alberto Mendez Rosado
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Objective: To describe some experiences in the diagnosis and management of Prader Willi Syndrome in the National Network of Medical Genetic Services in Cuba.

Methods: a Cuban medical literature search was conducted, mainly using Pubmed and Scielo databases. A strategy was designed using mainly terms: "Prader Willi Syndrome", "Genetic services" and Cuba. The articles chosen were published in English or Spanish languages which were accessed as full texts, besides documents from the National Network of Medical Genetic Services were also checked, evaluating their contents.

Results: The medical care for Prader Willi Syndrome patients was available throughout 169 municipalities, as well as provincial centers in all 15 provinces of the country, coordinated by the National Center of Medical Genetics of Cuba. Fifty Prader Willi patients were currently identified based on clinical criteria, chromosomal and molecular studies. All of them have received comprehensive medical care through genetic counseling provided by specialists of the National Health System.

Conclusions: The National Center of Medical Genetics has coordinated the medical care of Prader Willi patients and their families in Cuba allowing better prevention.

IV-3. "INCIDENCE AND CONSEQUENCE OF LARYNGOMALACIA IN INFANTS WITH PWS SEEN AT SEATTLE CHILDREN'S PWS CLINIC"

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Introduction: Growth hormone (GH) is started early in infants with Prader-Willi Syndrome (PWS) to improve tone, body composition, development, and growth. Concerns about sudden death in children with PWS started on growth hormone, hypothesized secondary to worsening obstructive sleep apnea (OSA) from adenotonsillar hypertrophy, resulted in guidelines for polysomnography (PSG) evaluation before and after starting GH. We reported 2 cases of worsening OSA after starting GH thought to be secondary to unmasked laryngomalacia. Laryngomalacia in PWS is not well described but it is associated with neuromuscular disorders and it may lead to exacerbation of OSA.

Methods: A retrospective review of infants seen at the Seattle Children's PWS clinic between October 2014 and July 2019 was done. Infants who had the majority of their care done at SCH were included. Those who had sleep endoscopy with flexible fiberoptic laryngoscopy (FFL) were further reviewed for diagnosis of laryngomalacia. Descriptive statistics were done to look at incidence of laryngomalacia and obstructive sleep apnea (OSA).

Results: A total of 23 cases (7 [30%] male, subtypes: 8 [35%] deletion, 11 [48%] mUPD, 1 [4%] imprinting center defect, 3 [13%] undetermined) were reviewed. Eight (35%) were evaluated with FFL between ages 5 and 40 months old (average 13.8 ± 12.2; median 10) for worsening or persistent OSA or dysphagia. Out of these, 7 (88% of FFL, 30% of total) were diagnosed with laryngomalacia (2 [29%] male, subtypes: 2 [29%] deletion, 4 [57%] mUPD, 1 [14%] imprinting center defect). Of the 23 infants, 8 (35%) had worse OSA after starting GH (GH effect could not yet be determined for 6 of the 23 patients). Of these 8 patients, 4 (50%) had laryngomalacia. Four of the 8 children (50%) had adenoidectomy with or without tonsillectomy to treat the OSA. Three children had surgical intervention of the laryngomalacia and 2 of these 3 had significant improvement of OSA after supraglottoplasty.

Conclusion: OSA can lead to significant morbidity in PWS. Growth hormone may unmask underlying laryngomalacia, possibly due to improved inspiratory force, causing worsening of OSA. Laryngomalacia is not well described in this population but our infant population had a 30% incidence overall, and 88%

incidence in those evaluated by sleep endoscopy. As only 35% of our patients had an evaluation with FFL, the incidence of laryngomalacia may be an underestimation. Although most infants grow out of laryngomalacia, if there are concerns of worsening OSA, then it is important to evaluate and consider treatment of this condition.

IV-4. "INCREASED BONE DENSITY WITHOUT CHANGES IN BONE MARKERS IN YOUTH WITH AND WITHOUT PWS WHO PARTICIPATED IN A 24-WEEK PHYSICAL ACTIVITY INTERVENTION"

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Introduction: During childhood, bone acquisition is affected by changes in hormones, height (Ht), lean mass (LM), physical activity (PA). This study compared bone mineral density (BMD), bone mineral content (BMC), and bone remodeling markers in youth with PWS versus youth with non-syndromic obesity (NSO) at baseline and after a PA intervention.

Methods: 30 boys & 24 girls participated, including 23 with PWS (Age: 11.1±2.7 y, Ht: 144.0 ±13.8 cm, LM: 29.4 ±10.6 kg, Fat: 44.8 ±10.4 %, 18 on growth hormone therapy) and 31 with NSO (Age: 9.6± 1.1 y, Ht: 147.3± 9.5 cm, LM: 33.2± 8.2 kg, Fat: 44.6± 6.2 %). Participants completed all measurements at baseline and after 24 weeks of a home-based game-centered PA intervention that included strengthening exercises twice a week. Dual x-ray absorptiometry scans of the hip, the lumbar spine (L1-L4) and full body determined BMC in g, BMD in g/cm2, and body composition (facility least significant change [LSC]: hip= .020 g/cm2; spine=.030 g/cm2). Bone markers included fasting serum bone-specific alkaline phosphatase (BAP) and C-terminal telopeptide of type I collagen (CTx). Changes over time were analyzed using general estimating equations. Percent changes in bone markers were also categorized as to exceeding or not the LSC (from inter- and intra assay coefficients of variation) and compared using Chi-square analyses.

Results: There were no differences at baseline for any spine parameters between the groups (p>.050 for all); spine BMC increased from 34.87±2.08 to 37.99±2.36 g, p<.001, and spine BMD from 0.909±0.023 to 0.939±0.026 g/cm2, p=.002 (LSC =.030). Hip differences between groups showed higher z-scores and BMC in NSO vs. PWS (p<.040). Hip BMD increased (0.882±0.021 vs. 0.918±0.026 g/cm2; p=.002; LSC =.020) as well as hip BMC (21.812 ±1.067 vs. 23.041±1.173; p=.012). Youth with NSO had higher BAP 139.07±6.41 vs. 108.28±9.19 U/L (p=.006) and similar CTx (2.07±0.11 vs.1.84±0.14 ng/dL; p=.193) than those with PWS at baseline. There were no group-by-time interactions for any bone marker (p>.425), or time effects (p>.209). There were no differences in the proportions of changes (pre-to-post) between the groups for BAP (12.2% increase, 61% decrease and 26.8 % no change; p=.130) or CTx (all youth: 48% increase, 36.6% decrease and 14.6% no change; p=.508). All youth gained LM (31.20±1.32 vs. 32.44±1.47 kg; p=.004) and Ht (145.7±1.6 vs. 147.9±1.8 cm; p=.002).

Conclusion: Youth demonstrated increases in bone parameters at or above the facility LSC. However, youth also increased Ht and LM, which may influence the gains in bone. During the 24-week youth PA intervention, youth participants potentially engaged in more exercises stimulating bone accrual (such as jumping and strengthening exercises); however, the lack of a control group precludes causality. In contrast to previous studies, youth with PWS had lower BAP than those with NSO; perhaps because 78% of them were on GH therapy. This study results suggest that youth with PWS can attain comparable changes in bone parameters over six months as those with NSO. Funded by US Army Medical Research and Materiel Command W81XWH11-1-076

IV-5. "IS THERE A 'FETAL PHENOTYPE' OF PRADER-WILLI SYNDROME?"

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Introduction: A "fetal phenotype" for Prader-Willi syndrome (PWS) has been proposed that may be identified in the third trimester of pregnancy based upon sonographic findings and maternal perception of fetal activity. Although the antenatal diagnosis of PWS has been made based upon sonographic findings, most of the findings have been described retrospectively in individuals diagnosed with the syndrome postnatally. We conducted a review of the reported findings to assess whether such a phenotype exists and may be used to identify fetuses for prenatal testing.

Methods: Perinatal data for individuals with PWS followed in the Texas Children's Hospital (TCH) PWS clinic was obtained by an IRB approved chart review and parental report. Prenatal ultrasound findings and perinatal findings were abstracted from published reports.

Results: A total of 703 PWS cases were included (102 cases from TCH and 601 cases from published reports). The most commonly reported finding was maternal perception of decreased fetal activity (60-92% of cases). Other reported findings included fetal growth restriction/small for gestational age (18-65%), polyhydramnios (23-46%), and malpresentation (21-64%). Abnormal positioning of the limbs was reported in a small number of cases. 21-81% were delivered by Cesarean section. A combination of findings was reported in 24-34% of cases in one study.

Conclusions: A small number of third trimester fetal findings are associated with PWS and may constitute a "fetal phenotype" for the disorder. However, there is a wide variation in the proportion of PWS cases exhibiting the features in different cohorts and the most commonly reported finding, maternal perception of decreased fetal movement, is subjective and nonspecific. Further study is warranted to determine the utility of prenatal findings in the diagnosis of PWS.

IV-6. "CHALLENGES IN MEDICAL MANAGEMENT OF OBESITY HYPOVENTILATION IN PRADER-WILLI SYNDROME"

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Introduction: Despite an extensive literature available on the syndrome, practical management of patients with Prader-Willi is poorly understood by well-trained clinicians who are generally encountering their first case. The author will delineate the most common and dangerous errors encountered in a consultation practice.

Methods: International clinical experience and consultation on cases of obesity hypoventilation in children and adults, eliciting recurring patterns of mismanagement.

Results: Treating physicians routinely fail to recognize the unique signs and stages of impending cardiopulmonary deterioration caused by obesity hypoventilation PWS: 1) nocturnal hypoxia; 2) non-pitting fluid retention; 3) daytime hypoxemia and dyspnea on exertion; 4) respiratory failure with or

without cor pulmonale. Non-pitting edema responds to exercise and not diuretics.Oxygen by nasal canula delivered at greater than 1 liter/minute without ventilatory support will suppress respiratory drive due to CO2 insensitivity in PWS while body positioning can improve ventilation. Medications for agitation may add to sedation and narcosis. Exercise is lifesaving and precipitates a brisk diuresis but may be hampered by hospital culture and mismanagement of disruptive behaviors. Uncertainty about food (lack of psychological Food Security) precipitates intense behavioral disruptions and interferes with care. The difficulty of communicating the basic elements of Food Security to multiple hospital staff members necessitates that an informed family member or professional caregiver be with the patient at all times which also reduces the nearly universal anxiety and disruptive behavior seen in PWS patients during hospitalization. OT and PT consultations can play a critical role even in the ICU as nursing staff are not accustomed to getting ICU patients out of bed and moving.

Conclusions: Obesity hypoventilation is a serious medical condition which is life threatening but when recognized and treated appropriately can be reversed at all stages. Unfortunately, it remains the case that people with PWS die because obesity hypoventilation is considered the inevitable end stage of the syndrome. The lessons of clinical experience are difficult to communicate and transmit but in the case of rare disorders, such as PWS, are lifesaving because inexperienced clinicians are the rule, not the exception. The interface of medical and behavioral knowledge of PWS is especially important since after early childhood behavioral problems interfere with good medical care in a majority of cases of hospitalization.

V. GENERAL MEDICAL ISSUES INCLUDING ORTHOPAEDICS

V-1. INVITED TALK: "THE ORTHOPAEDICS OF PRADER-WILLI SYNDROME"

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Some of the important hallmarks of Prader-Willi syndrome are related to musculoskeletal issues, such as developmental delay due to their hypotonia, flat footedness, and scoliosis. We will discuss how this problems present, and what different options are for treating them from the perspective of a pediatric orthopaedic surgeon with a large patient population of children with PWS. Topics will include strategies for addressing developmental delay, for gaining muscle and bone strength, and monitoring and treating disorders of the hips in children with PWS. Extended discussion will focus on spine deformities, including bracing, spinal casting, expandable spinal implants and spinal fusion. Anaesthetic and post-operative recovery concerns for children with PWS undergoing surgery will be covered.

V-2. "ROLE OF BODY CAST APPLICATION FOR SCOLIOSIS ASSOCIATED WITH PRADER-WILLI SYNDROME"

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Introduction: Approximately 40% of children with Prader-Willi syndrome (PWS) develop scoliosis, of which half develop their curves before 4 years of age, likely hypotonia related. Fifteen percent of all children with PWS will require surgical intervention. The complication rate for spine surgery in children with PWS is as high as 56%. This retrospective study evaluates the effectiveness of serial spinal casting to either correct a curve, or at least delay the necessity for expandable implant surgery, for infants and young children with PWS.

Methods: Since 2008, 32 patients with PWS had undergone spinal casting for scoliosis, of which 23 had a minimum of 2 years follow up after initial cast application. Criteria for casting included curves greater than 25°, or documented progression up to 25°, in children under 5 years of age. Radiographs were evaluated for Cobb angles and curve direction, rib-vertebral angle differences (RVAD), space available for lung (SAL), and Moe-Nash rotation for the initial pre-casting radiograph, and the last out of cast radiograph. Traction-release and in-cast radiograph were evaluated as well. Casts changes occurred every 2 to 4 months, dependent on the child's age. Curves were "cured" if their out-of-cast upright radiographs measured less than 15°, or less than 25° prior to three consecutive castings. Curves not "cured" would be controlled by casting or bracing until they were a suitable age for expandable spine implant surgery.

Results: The average age at initial cast application was 32 months (14 -64 months), an average of 8 casts (range 3-18) were applied, and the average follow up was 38 months. The pre casting Cobb angle of 58° (range 27-106°) was reduced to 37° (range 16-109°) at the latest followup. Curves were cured in 7 patients (6 uniparental disomy (UPD) and one deletion). Their average pre-casting curve was 42° (range 29° - 80°) which decreased to an average of 15° over 6 casts (3 - 8) spanning 17 months. At an average of 30 months since cast cessation, curves only increased to 18°. Three patients with large initial curves (54° - 109°) had placement of expandable spine implants an average of 51 months after initial cast, all three had deletions. Thirteen patients (5 UPD, 7 deletions, and one methylation defect) are either still undergoing casting or have been transitioned to bracing. Initial curves of 43° of less had an odds ratio of 37.5 for curve cure (P=0.0064).

Conclusions: Mehta style spinal casting is an important modality to treat infantile scoliosis in children with PWS. In general, curves less than 50° at cast initiation could be expected to reduce enough to allow graduation to a brace and subsequent weaning from brace. Curves larger than 50° could be controlled so as to postpone the need for surgery 3.5 - 5 years. This is a preliminary report, with a small sample size, due to the rarity of the PWS diagnosis. But it does appear that patients who start casting with a curve <50°, even at or slightly older than 3 years of age, have a favorable chance of a curve cure. It is encouraging that those with a cured curve continued to maintain a small curve over the brief followup period. There is a considerable concern, though, that once they reach early adolescents, the second peak incidence of scoliosis in PWS, that their curves may progress.

V-3. "HIGH PREVALENCE OF SCOLIOSIS IN A LARGE COHORT OF PATIENTS WITH PRADER-WILLI SYNDROME"

▸ Antonino Crinò[1], Michela Armando[2], Alessio Convertino[1], Danilo Fintini[1], Sergio Sessa[3], Sarah Bocchini[1], Sara Ciccone[1], Graziano Grugni[4]

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Introduction: Data about the prevalence of scoliosis in Prader-Willi syndrome (PWS) are not unequivocal, ranging from 15% to 86%. Furthermore, the role of growth hormone therapy (GHT) in the onset and progression of scoliosis remains controversial. In our study we investigated the prevalence and severity of scoliosis in a large group of

patients with PWS, with and without GH treatment, evaluating the effects of age, gender, body mass index (BMI) and genotype.

Methods: A cross-sectional study was performed in 180 patients with genetically confirmed PWS (99 deletion, 78 UPD, 3 unknown), 96 females and 84 males, aged 17.6±12 yrs (mean±SD) (range: 1.3-49.7, median: 15.5 yrs), BMI: 29.0±11.2 [99 subjects (55%) with BMI >2 SDS were considered obese]. One hundred forty-eight subjects underwent GHT (previously or currently), while 32 patients have never been treated.

Apart from anthropometric data, we performed an x-ray of the vertebral column. Assessment of scoliosis, including Cobb Angles (CA) measurements, was performed by the same senior spine surgeon. Scoliosis was defined as a CA of >10°. Moreover, scoliosis was classified using the Scoliosis Research Society classification (2006), in mild (CA 10-20°), moderate (CA 20-40°) and severe (CA >40°).

Results: One hundred forty-eight subjects (82.2%), 80 females (54%), were affected by scoliosis (mild: n.51; moderate: n. 47; severe: n. 50), predominantly with thoracolumbar curve, rarely with a double curve. Mean age at diagnosis of scoliosis was 7.1±6.3 yrs (range 0.6-30.4 yrs).

A corset was prescribed to 77 subjects at the age of 7.6±3.9 yrs (0.7-15.2 yrs) and was worn for 4.8±3.3 yrs. Twenty-six subjects (14,4%) with severe scoliosis and high risk of progression underwent surgery at a mean age of 12.8±4.7 yrs (range 4-27 yrs).

The mean age at starting of GHT was 4.7± 5.6 yrs (0.1-32 yrs). GHT was observed in a similar percentage in subjects with scoliosis (122/148 = 82.4%) and in patients without scoliosis (25/32 = 78.1%). No statistical correlation was found between scoliosis prevalence and genotype (deletion: 83.8%; UPD: 82%) as well as gender (females: 83.3%; males: 80.9%). Scoliosis was present in 86% of patients >18 yrs and in 79.2% of children and adolescents ($p<0,05$). Out of 99 subjects considered obese scoliosis was observed in 85% of the cases, while the prevalence in non-obese PWS was 79%.

Conclusion: In our large cohort of PWS, scoliosis affects most patients (148/180 = 82,2%), with a high prevalence of moderate-severe forms (68.2%). In the latter, 69,6% of subjects underwent conservative or surgical treatment. Apart from age, our data indicate that scoliosis is intrinsic to the syndrome, regardless of gender, BMI and GHT. Therefore, we suggest to perform a spinal x-ray regularly in all PWS subjects, starting from the first years of life, especially when the clinical and spinal examination is difficult due to the underlying obesity.

V-4. "COMPARATIVE COMORBIDITY BURDEN AMONG PATIENTS WITH PRADER-WILLI SYNDROME: A POPULATION-LEVEL COHORT STUDY"

▸ Diane E. Stafford[1], Justin W. Li[2], David Yin[2], Michael Yeh[3], Shawn Czado[3], Sina Aghsaei[2], Marissa Suh[2], Kevin Francis[2], & Shawn E. McCandless[4]

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Introduction/Background: Prader-Willi syndrome (PWS) is a rare, complex multi -system genetic disorder characterized by hyperphagia and abnormal food-related behaviors that contribute to severe morbidity and early mortality and to a significant burden on patients and caregivers. The hyperphagia seen in people with PWS can result in significant obesity. The objective of this study was to assess rates of comorbidities associated with obesity, including type II diabetes (T2D), cardiovascular disease (CVD), and sleep apnea (SA) in a large US PWS cohort versus a non-PWS cohort.

Methods: T2D, CVD, and SA conditions for privately insured PWS and non-PWS patients age <65 years were identified via ICD diagnosis codes in deidentified medical claims provided by IQVIA™ Health Plan Claims Data (1/2006 – 11/2018). Patients were required to have ≥12 months of enrollment, and patient observations were segmented into 12-month patient years.

Results/Discussion: 5,060 PWS and 31,093 non-PWS patient years representing 1,461 and 9,656 unique patients were eligible for analysis with comorbidity prevalence results below:

** To be compliant with HIPAA, figures representing patient counts <11 are not reported*

AGE	0-2		3-8		9-17		18-26		27-34		35-49		50-64	
GROUP	PWS	NON	PWS	NON	PWS	NON	PWS	NON	PWS	NON	PWS	NON	PWS	NON
COHORT		PWS	1187	PWS	1623	PWS	845	PWS	338	PWS	327	PWS	283	PWS
PATIENT-YEARS	457	1170	*	2624	8%	4389	19%	3809	27%	3370	27%	7748	27%	7983
T2D	*	*	11%	*	15%	*	29%	1%	44%	2%	60%	5%	78%	13%
CVD	25%	1%	22%	1%	17%	1%	18%	4%	18%	11%	15%	27%	16%	53%
SA	37%	*		0%		0%		0%		1%		3%		4%

The largest disparities between PWS and non-PWS T2D prevalence were observed in the 9-17 and 18-26 age groups. Manifestations of CVD in PWS patients ages 0-2 include higher rates of congenital CVD, even after excluding secundum atrial septal and patent ductus arteriosus. The proportion of PWS patients with SA who received continuous positive airway pressure or oxygen monitoring ranged from 38% to 71%.

Conclusions: Across all age groups, compared to non-PWS subjects, individuals with PWS experience markedly higher rates of CVD, T2D, and SA. The increased rate of CVD in the earliest age groups is consistent with previously observed increases in congenital heart defects with PWS. The frequency and early age of onset of hypertension, hyperlipidemia, T2D and SA emphasize the need for even more aggressive management of underlying drivers such as hyperphagia and the resulting obesity and metabolic dysfunction.

Funding source: Millendo Therapeutics provided funding support for this study.

V-5. "US PREVALENCE & MORTALITY OF PRADER-WILLI SYNDROME: A POPULATION-BASED STUDY OF MEDICAL CLAIMS"

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Introduction: Prader-Willi syndrome (PWS) is a complex developmental genetic disorder associated

with hypotonia, poor feeding in neonates, onset of hyperphagia in early childhood, and shorter overall life expectancy. Prior epidemiology studies of PWS have examined smaller populations, with only one study in a US population (Burd et al, 1990). The aim of this study was to provide a contemporary estimate of PWS prevalence and annual all-cause mortality in the US using a large administrative medical claims dataset.

Methods: PWS patients were identified between 2012-2014 via the presence of ≥2 claims with a diagnosis code for PWS on medical claims provided by IQVIA™ Health Plan Claims Data and CMS Medicare claims. PWS prevalence and mortality rates were calculated for 2014, and 2018 US census data was used to project rates for the total US population. The presence of select diagnoses and procedures suggestive of a life-threatening event (e.g., mechanical ventilation) with a patient's prompt disenrollment defined as death in the IQVIA data; vital status is indicated in Medicare data.

Results: Overall US diagnosed PWS prevalence was 2.7 per 100k persons (or 1 per 37,037), a prevalence of 8,870 patients in the US in 2018. Diagnosed PWS prevalence increased from 3.9 to 5.2 per 100k between the 0-2 and 3-8 age groups before decreasing in subsequent older age groups. The median age of PWS patients was 21 years. Annual age-adjusted all-cause mortality was 2.7%. Mortality was highest among diagnosed PWS patients ages 0-2 years and lowest among those ages 9-17 years (5.4 and 1.4% respectively), with annual mortality increasing in each subsequent older age group. The observed median age of death was 23 years (IQR 6-36).

DIAGNOSED PWS PREVALENCE AND MORTALITY IN 2018

AGE GROUP (YEARS)	0-2	3-8	9-17	18-26	27-49	>50	OVERALL
PWS PER 100K	3.9	5.2	4.5	4.2	2.5	1.1	2.7
UNIQUE PWS CASES	459	1,257	1,690	1,673	2,465	1,325	8,870
ALL-CAUSE MORTALITY	5.4%	3.0%	1.4%	2.1%	2.4%	4.5%	2.7%

Discussion: The diagnosed PWS prevalence of 1 per 37,037 persons estimated for the 2018 US population is comparable to the only other reported US prevalence estimate (ref?). As the current study describes diagnosed patients, it likely represents a lower bound of true PWS prevalence. Annual PWS mortality is ≥3 times higher than the overall US population (2.7 vs 0.8%). This rate appears unchanged from mortality estimates reported for PWS populations in the last several decades despite significant advances in genetic testing and the availability of growth hormone therapies in the US. Aggressive management of serious comorbid conditions, especially in younger PWS patients, should be a clinical priority.

Funding source: Millendo Therapeutics, Inc. provided funding support for this study.

VI. CLINICAL TRIALS FOR HYPERPHAGIA AND BEHAVIOUR

VI-1. INVITED TALK: "AN OVERVIEW OF CLINICAL TRIALS: DRUG DEVELOPMENT PROCESS IN PRADER-WILLI SYNDROME: CHALLENGES AND OPPORTUNITIES"

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Clinical trials have been fundamental in fostering the development of novel treatments in medicine and for understanding disease mechanisms. Since 2012, the number of clinical trials testing new drugs for PWS has been multiplied by four. Drugs with different mechanisms of action are being tested opening avenues for better understanding the biology underlying PWS. While this raises the hope that new treatments will be available in the near future, there are a number of challenges and barriers at each stage of the therapeutic development process that could impede successful clinical trials outcomes and access to meaningful therapies for individuals with PWS. An overview of the R&D stages and process for bringing a therapeutic candidate to clinical trial and access to patients as well as efforts undertaken by the PWS community to address challenges will be discussed in the context of the specificities of rare diseases and PWS.

VI-2. "TESOMET - A NEW TREATMENT OPPORTUNITY IN PRADER WILLI SYNDROME. RESULTS FROM PHASE 2A EXPLORATORY STUDIES IN ADULT AND ADOLESCENT PATIENTS"

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Introduction: Prader-Willi syndrome (PWS) is a debilitating, multi-faceted genetic disorder with no effective treatment. One of the hallmarks of this syndrome is insatiable appetite and constant drive to seek food. Tesomet, a combination of tesofensine (a noradrenaline, dopamine and serotonin reuptake inhibitor) and metoprolol (a □1-adrenergic blocker) has demonstrated a significant effect on satiety, appetite and food craving in several patient populations and is now also evaluated in PWS patients as a potential therapy for hyperphagia and overweight in this syndrome.

Methods and results: The Phase 2a exploratory study was conducted at two centers and in two parts: Part 1, a 12 week double-blind placebo-controlled study (randomized 2:1 with 0.5/50 mg of tesofensine/metoprolol in active arm), in nine adult patients; results were reported in 2018 and showed strong reduction in hyperphagia score (HQ-CT scale). Active arm: Reduction in hyperphagia score from 10 at baseline to a mean score of 0 at 12 weeks (mean score of 1 at 8 weeks). The mean weight loss was 6.75% in the active and 0.75% in the placebo arm. Four patients completed the study; noteworthy adverse events were exacerbation of pre-existing behavioral and psychiatric issues. No SAEs were reported. Part 2 of the study enrolled adolescent patients aged 12-18 and was a double-blind, randomized (2:1), placebo-controlled (0.125/25 mg tesofensine/metoprolol and matching placebos), 12-week study, followed by a 12-week open-label extension (OLE1; all patients on Tesomet 0.125/25 mg) and then another 12-week open-label extension (OLE2; patients on Tesomet 0.25/25 mg) if deemed eligible by the investigator and consented to participate. All patients were returning to the sites monthly. Primary endpoint was bodyweight, secondary endpoints hyperphagia score (HQ-CT), safety (AEs vital signs, ECG, labs), waist circumference, metabolic endpoints and PK. Nine patients were enrolled in the placebo-controlled part; 8 patients agreed to continue into OLE1 and 4 patients into OLE2. The treatment was in general well tolerated; the most frequently reported AEs were headache, insomnia, dizziness,

restlessness, palpitations, mood disorders. One non-related SAE was reported. There was no significant effect on the vital signs or laboratory parameters. Part 2 is still ongoing the full data will be presented at the meeting.

Conclusions: Based on data from this Phase 2a exploratory study Tesomet appears to have the potential to provide strong efficacy on hyperphagia and weight with a favorable risk/benefit profile.

VI-3. "TRIAL-IN-PROGRESS: ZEPHYR, A PIVOTAL PHASE 2B/3 RANDOMIZED, PLACEBO-CONTROLLED STUDY OF LIVOLETIDE, A NOVEL UNACYLATED GHRELIN ANALOGUE, FOR THE TREATMENT OF HYPERPHAGIA AND FOOD-RELATED BEHAVIORS IN PATIENTS WITH PRADER-WILLI SYNDROME"

▸ Soraya Allas[1], Pharis Mohideen[2], Thomas Delale[1], Vivian Lin[2], Michael Yeh[2], Nadège Tremel[1], Maithé Tauber[3]

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Background: Prader-Willi syndrome (PWS) is a rare, complex neuro-developmental genetic disorder characterized by hyperphagia and abnormal food-related behaviors that contribute to severe morbidity and early mortality and to a significant burden on patients and caregivers. There is no approved treatment for hyperphagia in PWS. People with PWS have increased circulating levels of the orexigenic hormone acylated ghrelin (AG) with a relative deficit of unacylated ghrelin (UAG). Livoletide (AZP-531) is a first-in-class UAG analogue that was previously shown in a Phase 2 randomized, double-blind, placebo-controlled study of 47 PWS patients to significantly improve hyperphagia, food-related behaviors, and metabolic parameters, and to be well-tolerated. [Allas S et al (2018) PLoS ONE 13(1): e0190849]

Objective: ZEPHYR (EudraCT 2018-003062-13; NCT03790865) is a pivotal Phase 2b/3 study that is designed to evaluate the long-term safety and efficacy of livoletide in patients with PWS.

Methods: The ZEPHYR study is currently being conducted in North America and Europe. In its Phase 2b portion, approximately 150 patients with PWS will be randomized to receive livoletide ~60Kg/kg, livoletide ~120 Kg/kg, or placebo, once daily by subcutaneous injection for a 3-month core period. Patients will then enter a 9-month extension period where all subjects receive livoletide. The Phase 3 portion will be initiated following results of the Phase 2b core period with patients randomized to livoletide at a single dose based on Phase 2b core data or to placebo. After 6 months of treatment in the Phase 3 core period, patients will enter the 6-month Phase 3 extension period where all subjects receive livoletide. Main entry criteria for ZEPHYR include genetic diagnosis of PWS, age 8-65 years, single primary caregiver available for the duration of the study, and body mass index (BMI) ≤65 kg/m2 for adult patients. Patients with type 2 diabetes with HbA1c ≤10% may be enrolled. Use of human growth hormone will be allowed if dosage is stable.

The primary outcome measure is the Hyperphagia Questionnaire-Clinical Trials (HQ-CT) score. The HQ-CT has been validated and is considered by regulatory authorities to be a valid primary endpoint. Secondary outcome measures include metabolic and body composition parameters such as fat mass as assessed by DEXA, BMI, and body weight in overweight/obese patients.

Results: The study is ongoing. Enrollment began in early 2019 and updates will be reported.

Conclusion: ZEPHYR is a pivotal study that will provide data on the long-term safety and efficacy of the novel UAG analogue livoletide on the treatment of hyperphagia and food-related behaviors in patients with PWS.

Funding source: Millendo Therapeutics provided funding support for this study.

VI-4. "EFFECT OF TOPIRAMATE ON EATING BEHAVIOURS IN PRADER-WILLI SYNDROME"

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Introduction: Prader-Willi Syndrome (PWS) is a rare genetic syndrome leading to severe behavioural disorders and mild cognitive impairment. The objective of this double-blind randomized placebo-controlled trial was to study the efficacy and tolerance of topiramate on behavioural disorders in patients with PWS.

Methods: Participants (aged 12 to 45 years) had genetically confirmed PWS and severe irritability/impulsivity, eating disorders and/or obesity, and skin picking. Thirty-two participants received a placebo (PBO), and 30 participants received topiramate (TOP) (50 to 200 mg/day) for 8 weeks. The primary outcome was the rate of responders using the Clinical Global Impression-Improvement (CGI-I) scale. The secondary outcome measures included the Aberrant Behaviour Checklist, the Dykens Hyperphagia Questionnaire (DHK), the Self-Injurious Behavior Scale (SIBS) and the body mass index (BMI).

Results: We found no significant difference in the primary outcome (the CGI-I): 9 (30%) patients were very much or much improved in the TOP group compared to 7 (22.6%) patients in the PBO group. However, the DHK behaviour and severity scores improved significantly more over time in patients treated with topiramate versus those receiving a placebo, with a significant dose-effect relationship. DHK scores were also significantly associated with genetic subtypes and hospitalization status. The effects of topiramate on eating behaviours remained significant after adjusting for genetic subtype and hospitalization.

Conclusions: Topiramate had therefore a significant effect on eating disorders, with a dose-effect relationship. Given the burden of eating disorders in PWS, we believe that topiramate may become the first psychotropic option within the global care of obesity in individuals with PWS.

VII. MENTAL HEALTH, BEHAVIOUR & COGNITION #1

VII-1. INVITED TALK: "MENTAL HEALTH AND BEHAVIOR IN PWS"

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The behavioral and mental health phenotype of PWS evolves across development, although the mechanisms for this progression are not understood. There are several processes that occur during typical brain development that may help to explain this progression, although the precise manner in which these mechanisms interact with the developing brain in PWS is less well understood.

These developmental mechanisms include:

1. Neurochemicals in the brain that take on different properties or effects across development, e.g., "the GABA brake" during the transition from the neonatal period to infancy;
2. Genomic imprinting mechanisms that may regulate how genes turn on and off across development;
3. The process of myelinization as the brain matures that allows areas of functional specialization, primarily in the cortex, to come "on line" and assert influence over previously connected "hard wired" subcortical regions;
4. Epigenetic mechanisms related to stress and environment that alter gene expression across development; and
5. The phenomenon of "critical periods."

There are several descriptive models derived from the phenomenology of PWS that have been developed to identify the emergence and progression of behavior in PWS, such as the appearance and course of temper tantrums and the nutritional stages of hyperphagia. Also, there are hypothetical constructs for understanding the behavioral phenotype: the reward hypothesis, the satiety and feedback deficit hypotheses; the autonomic dysregulation hypothesis, and the emotional salience hypothesis.

In this talk, an overview of the progression of behavior and mental health symptoms across development in PWS will be described with specific attention to phenomenology, models of brain development, evidence from brain imaging, and the current understanding of contributions from genetics, stress, and aging. Implications for prevention and timely management of symptoms will be discussed.

VII-2. "COGNITIVE FUNCTIONING IN CHILDREN WITH PRADER-WILLI SYNDROME DURING 8 YEARS OF GROWTH HORMONE TREATMENT"

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Introduction: Children with Prader-Willi syndrome (PWS) generally have mild to moderate cognitive impairment with an IQ between 60 and 70. Growth hormone (GH) treatment is a registered treatment for children with PWS and has been associated with cognitive benefits, attributed to the effects of GH and insulin-like growth factor on brain growth and development. Short-term data suggest positive effects of GH treatment on cognitive functioning in children with PWS.

Methods: In this prospective cohort study we longitudinally investigated the effects of 8 years of GH on cognitive functioning in 43 children with PWS. We also investigated whether starting GH early resulted in higher cognitive functioning after 8 years of GH. All children were treated with GH 1 mg/m2/day (≈0.035 mg/kg/day) and followed at the Dutch PWS Reference Center. Cognitive functioning was assessed by the Wechsler Intelligence Scale for Children (WISC). Vocabulary, Similarities and Block Design subtests were used and expressed as standard deviation scores (SDS). Total IQ (TIQ) was estimated.

Results: Forty-three children with PWS (29 girls) started GH at a median (IQR) age of 8.1 (6.6; 11.5) years. Estimated mean (95% confidence interval, CI) Block Design SDS changed from -2.2 (-2.6; -1.8) at baseline to -1.8 (-2.2; -1.4) after 8 years of GH (p=0.18), showing a modest trend towards an improvement of visuospatial skills in children with PWS. Similarities SDS changed from -1.5 (-2.1; -0.9) to -1.3 (-1.9; -0.7, p=0.66) and Vocabulary SDS remained similar, being -1.9 (-2.3; -1.4) at baseline and -1.9 (-2.4; -1.5) after 8 years (p=0.85), demonstrating that children with PWS develop abstract verbal reasoning and vocabulary at the same pace as healthy references. Mean estimated (95% CI) TIQ changed from 66 (60; 72) to 69 (63; 75, p=0.57).

We compared WISC results after 8 years of GH of the 43 longitudinally studied children who started GH during childhood to a separate group of 22 children from our Dutch PWS Cohort who started GH at a median (IQR) age of 1.4 (1.0; 1.8) years. We could not evaluate the longitudinal effects of 8 years of GH in the latter group, because WISC is not suitable for children younger than 6 years of age. After 8 years of GH, the 22 children who started GH during infancy scored significantly higher on the Vocabulary subtest (p<0.01), resulting in a higher estimated TIQ (p=0.04). Scores on the Block Design and Similarities subtests were similar between the two groups (p=0.48 and p=0.16, resp.).

Conclusions: Our results demonstrate that cognitive development during 8 years of GH in children with PWS remains similar and progresses at the same pace as healthy peers. Furthermore, early start of GH, in a critical period of neurodevelopment, might be beneficial for long-term cognitive functioning.

VII-3. "A GENOTYPE-PHENOTYPE ANALYSIS OF THE EFFECTS OF GROWTH HORMONE TREATMENT ON PSYCHIATRIC BEHAVIOR IN PRADER-WILLI SYNDROME"

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Introduction: This study aims to describe the frequencies of nine psychiatric behaviors found in PWS (depressed mood, anxiety, compulsions, skin picking, nail picking, compulsive counting, compulsive ordering, playing with strings, visual hallucinations, and delusions) as well as investigate their association with growth hormone treatment (GHT) for the most common molecular types: deletions (DEL) and uniparental disomy (UPD).

Methods: Retrospective guardian reported data were compiled from the Rare Disease Clinical Research Network's Natural History PWS and Morbid Obesity Clinical Protocol. Inclusion criteria included a confirmed diagnosis of PWS, 14+ years of age by last visit, and known GHT status. Out of a cohort of 355 individuals, 172 fulfilled criteria. Statistical analyses were performed using SPSS Statistics Software. Associations between use of GH and psychiatric phenotype were explored using Pearson Chi-Square tests and univariate and multivariate logistic regression analyses were employed to control for other confounding exposures. An interaction between GHT and genetic type was added to the univariate model.

Results: Among our cohort of 172 participants with PWS, 62.2% had DEL, 33.1% had UPD, and 4.7% had an imprinting center defect (ICD). Of those with DEL or UPD (n=164), 70.7% were on GH (72.9% and 66.7% respectively, p=0.404). A significant difference in skin picking frequency for those with DEL vs. UPD was identified (81.9% vs 63.2%, p=0.009). There was also a significant difference in anxiety frequency for individuals with DEL on GH vs. no GH cohorts (83.1% vs 16.9%, p=0.007). After adjusting for covariates, individuals with UPD had a higher presence of anxiety than those with DEL (OR=7.567, 95% CI: 1.781-32.146, p=0.006). Relative to those with DEL who did not use GH, those with UPD who used GH had a 3.25 fold increased presence of anxiety, whereas those with DEL who used GH had a 2.73 increased risk in anxiety. The other differences were not significant.

Conclusions: These results suggest that genotypic-phenotypic differences in psychiatric behaviors exist where skin picking is more frequent in those with DEL and GH was shown to have a higher association with increased anxiety for those with UPD vs. those with DEL. The data, however, are subject to a number of limitations. Psychiatric phenotypes are based only on guardian report. Furthermore, associations may reflect confounding from unmeasured covariates or chance due to multiple outcomes. As these results were unexpected in this preliminary study, more rigorous testing of a limited number of hypotheses as well as studies with more consistency in growth hormone treatment, onset, and duration are required before any conclusions can be reached and validated.

VII-4. "GRAY MATTER MICROSTRUCTURAL ALTERATION OF THE BRAIN IN INDIVIDUALS WITH PRADER-WILLI SYNDROME: A 7T MRI STUDY"

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Introduction: There is much research into common behavioral characteristics and developmental trajectories in individuals with Prader-Willi syndrome (PWS). This has contributed to our better understanding of behavior and mental health issues in PWS. Existing data suggest neurological underpinnings of both structural and functional alterations of the brain during its development in this population. We previously reported on white matter (WM) microstructural alterations using diffusion tensor magnetic resonance (MR) imaging. However, given the specific functional alterations relevant to the clinical behavioral patterns, structural connectivity should be simultaneously analyzed across gray matter (GM) and WM microstructures using an advanced diffusion imaging based on an ultra-high-field MR system. We hypothesized that developmental abnormalities of GM and WM microstructures exist in the brain of individuals with PWS.

Methods: Eleven individuals with PWS who manifested behavioral and developmental problems (age range: 15–42 years; male 8, female 3; Del 10, UPD 1), as well as age- and gender-matched typically developing controls participated in the study using a 7Tesla MR system. Diffusion characteristics—as indexed by neurite dispersion index (NDI), orientation dispersion index (ODI) using NODDI based on non-gaussian distribution assumption, and fractional anisotropy (FA) were assessed for cerebral cortical and subcortical structures. A whole brain analysis was performed complementary to a focused region-of-interest (ROI) correlation analysis with clinical behavioral pictures based on anatomically guided detection of cluster areas.

Results: We observed significantly reduced FAs in previously reported brain areas in individuals with PWS. Moreover, scattered increases in NDI and ODI were detected in multiple brain regions over the frontoparietal, temporal, and subcortical areas in the whole brain map. The ROI analysis subsequently identified significant correlations between maladaptive behavior scores and ODI ($p<0.05$, FWE corrected) in the bilateral frontal cortical areas in individuals with PWS compared to controls.

Conclusions: The observed altered diffusion characteristics indicate attendant developmental abnormalities within both GM and WM structures. These abnormalities were associated with observed clinical and behavioral patterns in individuals with PWS. The 7T study provides objective evidence regarding the effects of PWS on altered microstructural GM connectivity.

VII-5. "BILINGUALISM AND EXECUTIVE CONTROL: THE PWS POPULATION ON THE SPOTLIGHT AND... DOING WELL"

▸ Estela García-Alcaraz[1], Juana Muñoz-Liceras[1,2]

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Introduction: The executive Control (EC) capacity, which allows us to "successfully" carry out our daily life tasks, has been extensively scrutinized in Typically Developing (TD) individuals with the aim of understanding the relation between bilingualism and cognition. Inhibition, the capacity to focus on a specific task neutralizing non-relevant information, has been one of the processes that has attracted most attention. Given that bilinguals are used to have two languages activated at the same time and, for the most part, are constantly dealing and alternating between them, many studies have argued that this gives them an advantage over monolinguals to ignore non-relevant information, which, in turn, seems to result in better inhibition abilities (Valian 2015). However this "solid" bilingual "advantage" has lately been put in doubt arguing a possible publication bias towards positive outcomes of bilingualism over a neutral or negative effect of it (de Bruin et al. 2015). Thus, the main aim of this research was to study the inhibition capacity of bilinguals and monolinguals with a developmental disability with intellectual disability (ID), as is the case of PWS, to enlighten how bilingualism shapes their EC, since bilingualism is normally discouraged for this population without scientific evidence of its detrimental effect.

Method: 8 Spanish monolinguals and 7 Catalan-Spanish bilinguals with PWS completed two tasks intended to measure their EC capacity: a Flanker task (non-verbal) and a Stroop task (verbal). Both tasks were programmed in E-prime 2.0 and presented on a laptop computer. In the Flanker task five chevron sequences were presented and participants had to determine the direction of the central chevron (right or left) as quick as possible. Three stimuli conditions (32 items per condition) were included: (1) congruent (central chevron pointing to the same direction as the others chevrons), (2) incongruent (central chevron pointing to the opposite direction of the other chevrons) and, (3) control (only one chevron between four dashes -two in each side). In the Stroop task different color-colored words were presented and participants had to tell the font color in which the words were written. Three stimuli conditions (36 items per condition) were included: (1) congruent (color word and color font coincide), (2) incongruent (color word and color font do not coincide) and, (3) control (non-color word written in red, yellow or blue). For both tasks each trial consisted of an "Are you ready?" screen followed by a centered fixation cross presented during 500ms, followed by the target, which remained on screen until a response was provided. Participants responded using an USB numpad. Both reaction-time (RT) data and accuracy rates (ARs) were analyzed.

Results: Preliminary results do not reveal significant differences between groups neither for RTs nor for ARs in any of the two tasks. However, there was a main effect of condition in RT data in both tasks. In the case of the Flanker task, it revealed the following scale: Incongruent > Congruent > Control, and in the case of the Stroop task showed that incongruent items exhibited higher RTs than congruent or control items (Stroop effect). These findings are in line with previous findings from TD individuals.

Conclusions: These results show that bilinguals and monolinguals with PWS do not differ with respect

to EC ability, which is in line with the results of the limited previous research focused on bilingualism and IDs (Kay-Raining Bird et al. 2016), and challenges the extended practice to discourage these individuals to learn a second language (or a Heritage language) under the unfounded assumption that this could have a negative effect on their cognitive development.

VIII. MENTAL HEALTH, BEHAVIOUR & COGNITION #2

VIII-1. "FLEXIBLE SCHEDULING TO PREVENT THE DEVELOPMENT OF DISABLING RESISTANCE TO CHANGE: ACCEPTABILITY AND FEASIBILITY OF A DIGITAL INTERVENTION CO-PRODUCED WITH STAKEHOLDERS"

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Introduction: Negative emotional and beha vioural responses to altered routines or expectations – resistance to change - is common in individuals with PWS. It is a major trigger of behaviour problems [2-3], which may be disabling in their impact on the individual and their family. Growing evidence suggests that flexibility early-in-life may reduce later resistance by enhancing the development of task-switching, a cognitive process that appears to contribute to the effective management of change. This study aims to develop an intervention, which systematically increases variability in children's environments in a way that provides necessary structure for managing current behaviour challenges, alongside necessary flexibility for appropriate cognitive training.

Methods: An iterative collaborative design process was conducted with professionals (n=12) and families of children between 5-12 years with a diagnosis of PWS (n=15) or another neurodevelopmental disorder linked to resistance to change (n=21). Design specifications that would allow the intervention to meet families' needs were identified via individual interviews with caregivers (n=36). These criteria were used to create a paper prototype of the intervention, which was refined via focus groups with caregivers (n=13). A functional online prototype was then created, and tested at home by families in three stages (1-2 weeks) with iterative improvements being integrated throughout (n=12). Semi-structured individual interviews and questionnaires assessed acceptability and feasibility for all caregivers involved in testing. Focus groups with parents and children from three families further informed on these issues.

Results: All participants rated 'agreement' or 'strong agreement' on the potential benefits for their child, that it was an acceptable way to manage a difficulties with flexibility, and it would likely improve behaviours around change. Participants reported that the 'game-like' experience was exciting, it helped children manage changes they historically have found difficult, and that motivation was maintained.

Conclusions: Participants had an overall positive reaction to the intervention with reports that the integrated strategies supported parental confidence and management of current challenging behaviours. However, to increase motivation to engage long-term, children should have the capacity to personalise the graphics, and attainment of short-term goals should be noticeable for parents. With such refinements, the intervention has the capacity to provide families with remote-access to evidence-based behaviour principles, which can have an immediate positive impact on the experience of children and their families.

VIII-2. "A RANDOMISED CONTROL TRIAL TO EVALUATE THE IMPACT OF ENGAGEMENT WITH A TASK SWITCHING TRAINING COMPUTER GAME ON PEOPLE WITH PRADER-WILLI SYNDROME"

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Introduction: Resistance to change in expectations is part of the behavioural phenotype of Prader-Willi syndrome (PWS) and unexpected changes are one of the most common triggers of temper outbursts. Our own and others' previous research has demonstrated specific deficits in the executive process task switching in people with PWS. Importantly, work in PWS and other populations suggests a link between task switching deficits and resistance to change. We developed a computer-game to improve task-switching in children with PWS. An early prototype, appeared capable of improving task-switching skill in children with PWS. Here, we aimed to fully develop the prototype in an iterative collaborative process and evaluate how far engagement with the game could improve task switching skill and resistance to change behaviours.

Methods: "The Three Crowns" game was developed from our early prototype based on PWS families' experiences of engaging with the prototype, and over the course of an iterative process including three design workshops with young autistic people (autism is linked to resistance to change and including autistic people limited the exposure of people with PWS to the game before commencement of the evaluation, as such prior exposure could limit engagement).

In a double-blind placebo controlled design, randomised minimisation was used to allocate participants with PWS (n=30) to matched active training or placebo groups (same game, task-switching demands removed). Assessments were completed immediately prior to and following a 5-week game engagement period. Assessments included 4 direct tests of task switching (computer based) and parent report questionnaires on resistance to change, associated challenging behavioural responses, and behavioural indices of task-switching deficits. Parents also completed an online behaviour diary during a baseline and the engagement period. Following the engagement period, families were invited to take part in a 5-week follow up period, when all participants received the active version of the game, followed by an unstructured parent report interview on experience during the trial.

Results: Results varied across outcomes, and across individuals who engaged with the game over different durations. The efficacy and feasibility of the training will be discussed.

Conclusions: There may be some potential for computer games to be used to improve task switching and associated behavioural problems in some people with PWS. However, timing, dosage and individual cognitive and behavioural profiles may affect outcomes and more research is needed to allow such an approach to be appropriately targeted.

VIII-3. "SPECIFIC FEATURES IN THE EXPRESSION OF EMOTIONS IN CHILDREN WITH PRADER-WILLI SYNDROME : WHAT ARE THE CONSEQUENCES FOR EMOTION ABILITIES AND SOCIAL ADJUSTMENT?"

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Introduction: People with Prader Willi Syndrome (PWS) have great difficulties of social adaptation that could be explained by disturbances of emotional competencies (i.e. ability to use emotions daily). However, we currently have incomplete knowledge about the emotional functioning of people with PWS and even more about its development during childhood. In particular, the emotional expression abilities (facial, bodily) have never been investigated while they are at the foundation of the establishment of interpersonal relationships and thus of social adaptation. In addition, the motor and cognitive difficulties - characteristic of the PWS - could further impair these abilities. The objective of this study was, among other things, to explore precisely the expression abilities of children with PWS.

Method: Twenty-five French children with PWS aged 5 to 10 years were assessed for 1) their emotional facial reactions to a funny video-clip and 2) their ability to deliberately produce the facial and bodily expressions of joy, anger, fear and sadness. Their productions have been compared to those of two groups of children with typical development (TD); matched to PWS children, on the one hand, by chronological age, and, on the other hand, by developmental age.

Results: The results showed that children with PWS presented as many emotional facial reactions as TD children. However, many ambiguities have been noted in their facial expressions, making them particularly confusing. Precisely, we observe in expressions a lot of mixture of different emotional patterns (e.g., some parts of disgust or fear patterns in laughter expressions). In addition, it has been observed that the deliberate emotional productions of PWS children have been particularly minimalist and confused.

Conclusions: This study was able to highlight the existence of particularities in the expression of emotions in PWS children. These results shed new light on the emotional functioning in the PWS and consequently on the adaptive abilities of these people in the daily life.

VIII-4. "PRACOM 2 PROJECT: STUDY OF THE EMOTIONAL ASPECTS ASSOCIATED TO BEHAVIORAL AND COGNITIVE TROUBLES IN THE PRADER-WILLI SYNDROME"

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Introduction: Prader-Willi Syndrome (PWS) is a rare genetic pathology characterized by several behavioral and cognitive disorders (Whittington & Holland, 2017). Temper tantrum is one of the most frequent maladaptive behaviors in the PWS (Rice et al., 2018) associated with emotional lability (Woodcock et al., 2011) and widely described in the literature. However emotional features associated to this behavior and their relationships with cognitive and social aspects are less known. The project PRACOM 2 is part of a wider project called PRACOM (PRAder-Willi Communication) which aim is to identify emotional characteristics of adults with PWS that are associated to their behavioral disorders (especially anger behavior) which can be an obstacle for social integration and communication. In PRACOM 2 we focused as well on patient's cognitive abilities to process emotional information and on the repercussions for the well-being of parents.

Methods: For the project, we will include 30 patients with PWS, 30 adults without pathology (matched on age and sex) and 30 parents of patients (one of them). Three sessions of evaluations (questionnaires and cognitive tasks) of 1h30 are proposed to the two groups of participants and one remote session (questionnaires and interview) for the patient's parents. Questionnaires of emotional regulation, emotional lability, emotional reactivity, irritability and depression are used to characterize emotional features of adults with PWS. The evaluation of behavioral disorders (e.g., hyperphagia, temper tantrum) is also made through questionnaires. Moreover, the well-being of parents is evaluated by an interview about their needs and questionnaires about their quality of life and burden. Finally, to examine the cognitive abilities of people with PWS to process emotional information, we propose an emotional lexical decision task. In this task, participants have to decide if letters presented on a computer screen represent a word (e.g., family) or not (e.g., faurt). Words can reference joy, sadness, anger or neutral. If patients can process efficiently emotional information, recognition times could differ according to the emotional content of words compared to neutral ones.

Results: First results on 15 adults with the SPW (mean age = 32,33) and 25 adults without pathology (mean age = 32,16) have showed that people with PWS demonstrated a higher level of depression, irritability, emotional lability, emotional reactivity and difficulty to suppress their affect compared to people without the pathology. Moreover, emotional lability and irritability were the only factors associated to behavioral troubles. Furthermore, a high-level of emotional lability, depression and irritability of patients negatively impact the quality of life and burden of parents. Finally, results of the emotional lexical decision task showed that patients process emotional words efficiently. Overall, these first results suggest difficulties in PWS patients to control their affective state but good abilities for processing emotional information.

Conclusions: Benefits of the PRACOM 2 project concern the improvement of the knowledge related to the emotional functioning of adults with PWS and the factors regulating behavioral disorders. Among others, this will allow a better management of the syndrome by family and clinical staff.

CLINICAL AND SCIENTIFIC CONFERENCE: POSTER ABSTRACTS

I. GENETICS, EPIGENETICS & ANIMAL MODELS

POSTER #1 NARROWING THE CRITICAL DELETION REGION OF PRADER-WILLI SYNDROME: EXTREMELY MILD PHENOTYPE CAUSED BY AN EXTREMELY SMALL DELETION OF THE PRADER-WILLI REGION

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Introduction: Prader-Willi syndrome (PWS; OMIM #176270) is a rare condition (1:25.000 births) affecting many organ systems. PWS is characterized by mild to severe mental retardation, extreme appetite (hyperphagia) and pituitary hormone deficiencies. Usually, PWS occurs due to the absence of expression of a cluster of paternally expressed genes located in the PWS region on chromosome 15q11.2-q13, either due to uniparental maternal disomy (mUPD, 30%), an imprinting center defect (ICD, <5%) or a paternal deletion (DEL, 70%). The deletion class is typically subdivided into Type 1 and Type 2 based on their proximal breakpoints. Despite PWS being a well-characterized genetic disorder, the role of the specific genes contributing to various phenotypic features are not well understood. Methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) is a technique that detects copy number changes and aberrant DNA methylation. We describe a patient with PWS who had an extremely mild phenotype, in whom we have applied MS-MLPA to elucidate the deletion subtype.

Methods: We collected genetic and phenotypic data of all 120 adults with PWS attending the outpatients clinic for adults with PWS. In one patient with an extremely mild phenotype, we performed methylation specific PCR which revealed a paternal deletion.

In order to find an explanation for his extremely mild phenotype, we additionally carried out MLPA using kit ME028-B2 PWS/AS (MRC Holland) to delineate the deletion.

Results: Among 120 patients attending the outpatients clinic for adults with PWS, genetic analysis revealed ICD in 3%, mUPD in 27% and a deletion in 70%. One patient with a deletion had an extremely mild phenotype. Although he had had hypotonia and feeding difficulties at birth, at adult age he had normal IQ, almost no hyperphagia and he had even obtained his driving license. He had only mild autistiform features and led a nearly normal social life. He did not have growth hormone deficiency or adrenal insufficiency. Whereas severe hypogonadism is present in almost all PWS adults, he had normal pubertal development. In order to find an explanation for his extremely mild phenotype, we carried out MLPA, which showed an abnormal pattern for 21 consequent probes located in SNRPN and UBE3A. For all other probes, a normal pattern was seen.

Conclusion: We report a PWS patient with a remarkably mild phenotype, caused by an atypical, unusually small deletion. The deletion only affected SNRPN and UBE3A and none of the other genes in the Prader-Willi region. Functional impact of this deletion will increase our knowledge of the pathophysiology of Prader-Willi syndrome

POSTER #2 HOMOZYGOUS SNRPN POINT MUTATION AS A POTENTIAL NEW CAUSE OF PRADER-WILLI (LIKE) SYNDROME

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Introduction: Prader-Willi syndrome (PWS) is generally believed to be caused by loss of expression of an entire cluster of paternally expressed genes within the PWS region on chromosome 15, due to deletion, uniparental disomy or imprinting center defects. We describe a unique patient with the complete spectrum of PWS features, in whom these regular causes were excluded. Additional genetic testing revealed a homozygous point mutation in SNRPN (one of the genes located in the PWS region), which was located in a large homozygous region (the parents were first-degree relatives). SNRPN encodes snRNP polypeptide N (SmN), which is highly expressed in the brain and is involved in neurite outgrowth, neuron migration and distribution of dendritic spines in mice. However, the precise role of SNRPN in the development of the PWS phenotype still remains largely unknown. This patient is unique, because point mutations in a single gene have never been described before as the cause of PWS.

Methods: In the index patient, we performed methylation testing, Multiplex Ligation-dependent Probe Amplification (MLPA) analysis, SNP array and obesity gene panel analysis, targeted analysis of 52 obesity-related genes using automated sequencing.

Results: In the 46-year-old female index patient, genetic diagnosis of PWS was initially rejected after regular genetic tests for PWS showed normal results. We performed additional obesity gene panel analysis, which identified a homozygous point mutation in SNRPN, located in a large homozygous region on chromosome 15.

Conclusion: Until now, it was generally accepted that Prader-Willi syndrome could only be caused by functional loss of an entire cluster of genes within the PWS region on chromosome 15q11.2-q13. The unique finding of a homozygous point mutation in a single gene of this region (SNRPN) in a patient with virtually all features of PWS, contributes to the unravelling of the pathophysiology, and the role of SmN in PWS.

POSTER #3 ALGORITHM FOR THE DIAGNOSIS OF PRADER-WILLI SYNDROME IN CUBA.

▸ Luis A. Méndez Rosado[1], Odalis Molina Gamboa[1], Lainet Merencio Santos[2], Luanda Maceiras[1], Anduriña Barrios Martínez[1], Paulina Araceli Lantigua Cruz[3].

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Introduction: Prader Willi syndrome is a complex genetic disease caused by different genetic mechanisms that result in the physical or functional

absence of a group of genes on chromosome 15. Clinical analysis can be complicated when it comes to Prader-Willi syndrome because to the existence of phenotypic traits that may be common to other genetic abnormalities.

Objective: Describe a working algorithm for the diagnosis of Prader Willi disease.

Result: 62 patients with clinical suspicion of Prader-Willi syndrome were analyzed. 31 individuals with the disease were detected, through studies of conventional karyotype, FISH and methylation analysis. 28 presented the deletion on the maternal chromosome 15 corroborated by FISH.

Conclusions: Through the correct clinical analysis of the patient, the use of the methylation test and the FISH technique, an accurate diagnosis of the disease is achieved in a number of cases despite the genetic heterogeneity that accompanies the clinical manifestations in these children.

POSTER #4 CLINICAL AND GENETIC CHARACTERIZATION OF A GROUP OF CHILDREN WITH PHENOTYPE SUGGESTIVE OF PRADER-WILLI SYNDROME

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Introduction: Prader-Willi syndrome (PWS) is a genetic disorder characterized by hypotonia and feeding difficulties in infancy, followed by hyperphagia, hypogonadism, mental retardation, and short stature. Its clinical features tend to be confused with several other disorders and its diagnosis is not always as early as it could be.

Methods: A review of 15 clinical histories of children (7 males and 8 females) with features of Prader-Willi syndrome was performed in order to delineate the main phenotypic signs and genetic defect.

Results: Prenatal history of fetal inactivity and breech presentation was found in 66% of patients, while severe hypotonia and feeding problems in neonatal period were present in 100%. Poor sucking and weight gain in early infancy and hyperphagia after 6 months were found in all cases with the result of 6 patients (40%) with moderate obesity and 9 (60%) with a severe one. All patients had small hands and feet, typical facial features and neurodevelopmental delay, but only 4 females had hypogonadism while all males had it. Intellectual disability was described in all the eldest patients. The mean age at diagnosis was 2 years old ranging from 15 days to 18 years. Despite some problems with cytogenetic and molecular analysis of PWS that makes difficult the diagnosis, a de novo deletion of 15q11-q13 was found in 4 patients and methylation defects in another 4 suggesting maternal uniparental disomy. In one patient a balanced chromosomal translocation involving 15q11 was detected. The rest of the patients are still pendants of molecular confirmation.

Conclusions: Prader-Willi syndrome should be suspected in any infant with early severe hypotonia and feeding problems. Cytogenetic and molecular studies should be performed in these cases in order to confirm or deny the diagnosis.

POSTER #5 MOLECULAR DIAGNOSIS OF PRADER-WILLI SYNDROME IN CUBA

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Introduction: Prader-Willi Syndrome is a genetic disorder caused by the loss of function of genes in the 15q11.2–q13 region of the paternal chromosome. It is characterized, among other manifestations, by hypotonia, hypogonadism, hyperphagia, short stature and delay of neurodevelopment. DNA methylation analysis is a molecular technique that allows the study of this disease and thus the diagnosis of any of the main genetic mechanisms that cause it, such as, deletions, uniparental disomy and imprinting defects at chromosome 15. This study aims to perform the molecular diagnosis of Prader-Willi Syndrome through the methylation-sensitive polymerase chain reaction (MS-PCR).

Methods: Genomic DNA isolation of a total of 66 blood samples, mouth scraping or amniotic fluid by manual or automated extraction was performed. Subsequently, the extracted DNA was treated with sodium bisulfite through the EZ DNA Methylation kit for the next realization of the polymerase chain reaction using specific primers that allow specific amplification of maternal alleles and paternal of the SNRPN gene. The results were visualized under ultraviolet light in Agarose MS gel at 3% dyed with ethidium bromide.

Results: 100% of the samples were diagnosed, with 40 negative and 26 positive individuals, molecularly confirmed by conducting this study, which also enables the availability of a molecular diagnostic method in the country.

Conclusion: The MS-PCR technique is a fast, economical and highly sensitive method that enables molecular diagnosis of Prader-Willi Syndrome.

POSTER #6 CHROMOSOMAL ABERRATIONS DETECTED IN PATIENTS WITH PRADER WILLI LIKE PHENOTYPE

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Introduction: Prader Willi syndrome is a genetic disorder due to the lack of expression of paternal genes on chromosome 15q11-13 region. Clinical manifestations include neonatal hypotony, hyperphagia, obesity, hypogonadism and a intellectual disability in variable grade. Nonetheless, an important percentage of cases defined as Prader Willi like syndrome is suspected there is not a genotype/phenotype correlation. Objective: To describe the genetic findings in patients with Prader Willi phenotype lacking any alterations in region 15q11-13.

Methods: We studied 62 patients with Prader Willi syndrome phenotype by karyotype, FISH and PCR-based methylation test. A search for cases published during the period 2005-2018 was performed. Selection included the Pubmed database (www.pubmed.com) and Scielo (www.scielo.br). Those cases where karyotype, FISH, PCR-based methylation test and CGH failed to confirm the clinical diagnosis were selected and compared with the results of patients included in our study.

Results: International scientific literature reports until 80% of diagnosed cases as Prader Willi like syndrome. Chromosomal alterations involve the

following chromosomal regions: 6q, Xq, 10q, 12q, 1p, 2p, molecular pattern compatible with Angelman's syndrome and maternal uniparental disomy in chromosome 14. It was observed 50% of cases in our investigation with Prader Willi like syndrome, without alterations seen by classical cytogenetic.

Conclusions: Lack of confirmation for a chromosomal region 15q11-13 alteration makes a deep clinical delineation, classical cytogenetic test and molecular studies throughout the genome are powerful tools indispensable for genetic diagnosis in patients with a Prader Willi like syndrome.

POSTER #7 INTERNATIONAL PRADER-WILLI SYNDROME FREE DIAGNOSIS PROGRAMME

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Prader-Willi syndrome (PWS) is a rare genetic disease where an early diagnosis can have a significant impact on the life expectancy of the patient. Whilst there are specific pharmacological treatments that can improve the quality of life of PWS patients, like hormone replacement therapy, the most important part of the therapy is appropriate dietary restrictions. Diet alone can significantly improve the life expectancy in PWS patients and it can be implemented regardless of the socio-economic conditions. This is why we need to make sure that every child with PWS has a confirmed diagnosis as early as possible.

Since 2004 the "Mauro Baschirotto" Institute for Rare Diseases (BIRD), together with the International Prader-Willi Syndrome Organisation (IPWSO), offers free diagnostic tests for PWS for the countries where such service is not currently available. This experimental program is intended as a means for medical doctors to molecularly confirm or eliminate the clinical diagnosis of PWS in their patients. Since the beginning of this initiative 530 samples from 44 different countries have been analyzed, identifying 192 cases of PWS. The analyses use the methylation specific polymerase chain reaction (MS-PCR) method and the sample sending procedure was designed to be as straightforward as possible using dried blood spots (DBS) on Whatman type filter paper. In addition to this testing, the laboratory at BIRD has trained two laboratory directors in the use of the testing methodology so that they may introduce testing in their own country.

The initial procedure relied purely on the referring medical doctor to determine the suspected cases but the resulting percentage of positives was below our set goal of 40% (33% in 2005). During the ensuing years various steps were introduced to help in the clinical diagnosis and improve the selection of the most likely cases of PWS. This resulted in the increase of positives to more than 40% (54% in 2018). The current procedure includes a clinical data collection form and a pre-approval step before a sample can be accepted for testing. The data collection form includes the international guidelines for the clinical diagnosis of PWS and contains fields for key information that can help in the diagnosis of PWS.

An ongoing project is the adaptation of the methylation specific multiplex ligation-dependent probe amplification (MS-MLPA) method for international PWS testing, with an aid from MRC Holland, the company that developed and produces the PWS MS-MLPA diagnostic kit. In comparison to the currently used MS-PCR method, MS-MLPA allows the discrimination between deletion and non-deletion subjects with PWS. In addition, this test can also give an estimate of the size of a deletion. Special focus is given to the quality of the samples and the DNA extraction method, as MS-MLPA is very sensitive to variations between the tested DNA samples and the calibration controls. Additional efforts will be made to raise awareness of this initiative to as many people as possible. The guidelines are being further improved and a new separate documentation specifically aimed at families is being introduced to help them understand the importance of these tests for the health of their loved ones with PWS.

POSTER #8 INVESTIGATING THE CONTRIBUTION OF THE PRADER-WILLI SYNDROME CRITICAL INTERVAL TO BEHAVIOUR AND COGNITION

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Introduction: The core features of Prader-Willi Sy-ndrome (PWS) are hypotonia and slow growth rate in infancy, followed by severe hyperphagia, which can lead to obesity throughout childhood and adulthood. Individuals with PWS also exhibit mild to moderate learning disability as well as a range of behavioural and psychiatric phenotypes suggestive of elevated anxiety, impaired attention, and psychosis.

PWS is caused by loss of function mutations affecting paternal expression of genes from the imprinted cluster on chromosome 15q11.2-q13. Two non-coding RNAs, SNORD116 and IPW within this cluster are collectively known as the PWS critical region (PWS-cr), as deletion of the PWS-cr is sufficient to lead to PWS. However, while PWS-cr contributes heavily to the core features of PWS, including the hyperphagia and hypotonia, it is unclear whether, and to what extent, it plays a role in the behavioural and psychiatric phenotypes typical of the syndrome. Our previous studies of a full genetic mouse model for PWS (PWS-IC) shows deficits in endophenotypes of relevance to the behavioural and psychiatric problems, including hypoactivity, sensory-motor gating, attention, and impulsivity. The aim of this study is to characterize the behaviour of a PWS-cr+/- mouse model in order to assess whether the PWS-cr plays a role in the manifestation of these behavioural and cognitive abnormalities.

Methods: PWS-cr+/- mice were assesed as adults (8-weeks onwards) on measures of locomotor activity, anxiety (open field and elevated plus maze), sensory motor-gating (acoustic startle and prepulse inhibition tests). The 5-choice serial-reaction time task (5CSRTT) was used to assess attention and impulsivity. An RNA sequencing study on brain tissue from the PWS-cr+/- mouse model is being performed in order to examine the effect of PWS-cr on gene expression and post-transcriptional modifications in the brain.

Results: Loss of the PWS-cr led to some subtle behavioural changes. While there was no difference in behaviour between genotypes on the elevated plus maze, the results from the open field were suggestive of elevated anxiety in the PWS-cr+/- mice. No differences between genotypes were found in locomotor activity or in habituation to the environment. The PWS-cr+/- mice also exhibited reduced acoustic startle response compared to wildtype, but no differences in pre-pulse inhibition of the startle response. Results from the 5CSRTT indicated no effect of genotype on attention, but indications of defective learning and increased impulsivity in the PWS-cr+/- mice.

Conclusions: Overall, the PWS-cr+/- mice exhibited elevated anxiety, reduced acoustic startle response and increased impulsivity. However, the absence of the PWS-cr interval did not have an effect on locomotor activity, attention and pre-pulse inhibition. This is in contrast to the behavioural profile of the "full" genetic PWS-IC mouse model. These results suggest that whilst the PWS-cr interval might play a subtle role in some of the behavioural phenotypes seen in PWS, it does not lead to the behavioural and cognitive endophenotypes associated with psychiatric illness seen in a "full" genetic mouse model for PWS.

POSTER #9 SERUM CONCENTRATIONS OF ASPROSIN IN CHILDREN PRADER-WILLI SYNDROME: ASSOCIATION WITH GLUCOSE AND INSULIN RESISTANCE

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Introduction: Asprosin is a newly discovered hormone produce by the white adipose tissue that stimulates glucose production and is correlated with insulin resistance. Asprosin increases after fasting and decreases with food intake, utilizing the same signaling pathways, Neuropeptide Y/Agouti-Related Peptide (NPY/AGRP), as ghrelin. Both asprosin and ghrelin are orexigenic hormones. Prader-Willi syndrome (PWS) is a unique clinical model of disordered satiety and paradoxical hyperghrelinemia. However, it is not clear if asprosin levels are altered in children with PWS. Therefore, the aim of our study was to measure the concentrations of serum asprosin in children with PWS and BMI-z score matched children and to assess its relationship to glucose, insulin resistance, ghrelin, leptin, and percentage of body fat.

Methods: Fasting and 1-hour post meal serum concentrations of asprosin were measured using an enzyme-linked immunosorbent assay kit (Catalogue No. abx257694; abbexa, Cambridge, UK) in ten children with PWS (9F/1M, 5.1-17.9 years) and seven BMI-z score matched children (1F/6M, 6.8-17.1 years). Hormones including: glucose, insulin, acyl ghrelin and leptin were also measured. Height was measured to the nearest 0.1cm using a wall-mounted stadiometer and weight was measured to the nearest 0.1kg using the calibrated scale. Body composition (percent body fat) was measured by air displacement plethysmography. Homeostatic model assessment insulin resistance (HOMA-IR) was calculated as fasting glucose (mg/dL) × fasting insulin (μIU/mL) ÷ 405. Groups were compared for %fat, fasting and 1 hour level of hormones using the Mann-Whitney U Test; Wilcoxon Signed-Rank Test was used for within group comparison of fasting asprosin and 1-hour post meal asprosin. Correlation between each fasting and post-meal asprosin, demographic and other fasting hormone levels were determined using Spearman's Rank-Order correlation, considering a critical significance value of $p<0.05$.

Results: PWS and controls were of similar age and BMI-z score. Children with PWS had lower fasting levels of glucose ($p = 0.04$) and showed a trend for lower HOMA- IR ($p = 0.05$). Fasting asprosin, insulin, percent body fat and leptin were comparable between groups. However, children with PWS had higher fasting levels of acyl ghrelin ($p = 0.02$) compared to BMI-z score matched children. Fasting asprosin and 1-hour post meal asprosin did not differ between children with PWS and BMI-z matched children ($p = 0.37$ and $p = 0.5$, respectively). Fasting asprosin was positively associated with percent body fat and BMI-z score ($rs = 0.70$, $p = 0.04$ and $rs = 0.90$, $p <0.01$) in children with PWS, but not in BMI-z score matched children.

Conclusion: This study indicates that fasting acyl ghrelin is higher and fasting glucose is lower while HOMA-IR trend to be lower in children with PWS, suggesting that children with PWS are more insulin sensitive than BMI-z score matched children. Serum asprosin was positively associated with adiposity-related parameters in children with PWS, including percent body fat and BMI-z score; no significant correlations were found in controls. Future larger-scale studies in children with PWS and obesity (with and without insulin resistance) is needed to confirm our findings.

POSTER #10 GH STIMULATED LEVELS DURING TRANSITION PHASE IN PRADER-WILLI SYNDROME

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Introduction: In the general population, GH deficiency (GHD) during the transition phase is associated with deterioration of body composition, metabolic alterations and reduced bone mineral density. Subjects with Prader-Willi syndrome (PWS) have reduced muscle mass, increased risk of cardiovascular disease and osteoporosis, similarly to what has been observed in patients with non-syndromal GHD. Consequently, assessment of the GH status from late teenage years until 6-7 years after achievement of final height may be particularly helpful in the management of PWS in this particular period.

Methods: A cross-sectional study was performed in 133 patients with genetically-confirmed PWS (85 del15, 46 UPD15, 1 ID, 1 met+), 69 females, aged 19.8±2.4 yr (mean±SD), BMI 35.6±10.4. Ninety-three subjects had previously undergone GH treatment (69.9%), and withdrawn in all cases at least 6 months before starting the study protocol. Pituitary GH secretion was evaluated by standard dynamic testing with GHRH+arginine. In order to define GHD, we adopted the BMI-related diagnostic cut-off limits of GH peak (GHp) (Corneli et al, Eur J Endocrinol 2005). In addition, the cut-off limit specific for transition phase (GHp <19 μg/L] (Corneli et al, Eur J Endocrinol 2007) was used. Serum IGF-I levels were determined at baseline.

Results: According to the BMI cut-off limits, 31 of 84 (36.9%) obese (BMI= 44.6±6.7) PWS subjects could be defined as GHD (GHp<4.2 μg/L), as well as 7 of 24 (29.2%) overweight (BMI= 27.6±1.4) patients (GHp<8 μg/L) and 5 out of 25 (20.0%) normal weight (BMI= 22.4±2.2) individuals (GHp<11.5 μg/L). Overall, GHD was present in 32.3% of the subjects. Serum IGF-I was <-2 standard deviation scores (SDS) in 51 patients (38.3%). Twenty-five subjects had both the pathological GHp and IGF-I <-2 SDS (18.8%). Finally, 99 individuals showed GHp <19 μg/L (74.4%).

Conclusion: Our results indicate that GHD may be present in a significant percentage of PWS patients during transition phase. The challenge is to demonstrate that GH therapy after completion of linear growth will lead to an improvement in morbidity and mortality in PWS individuals. Thus, a re-evaluation of the GH secretory pattern may be beneficial in all PWS patients after achievement of final height.

POSTER #11 EFFECT OF GROWTH HORMONE TREATMENT ON GLUCOSE TOLERANCE IN YOUNG ADULTS WITH PRADER-WILLI SYNDROME

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Introduction: in children with Prader-Willi syndrome (PWS), the benefits of growth hormone (GH) treatment are well established. GH has substantially changed the phenotype of children with PWS. Currently, when young adults with PWS have attained adult height (AH), they have to stop GH treatment. Adults with PWS are predisposed to develop impaired glucose tolerance (IGT) and diabetes mellitus type 2 (T2DM). Reports on the prevalence of T2DM vary from 7-24% in adults with PWS. Studies in adults with PWS showed positive effects of GH on body composition and metabolic health parameters, but GH is known to induce insulin resistance, which might lead to IGT and T2DM.

Methods: in this open-label, prospective study we investigated the effect of continuation of GH after AH attainment on glucose homeostasis in 42 young adults with PWS. All young adults received 2 years of GH after AH attainment in a standard dose of 0.33 mg/m2/day (~0.035 mg/kg/day). An oral glucose tolerance test (OGTT) was performed every year. IGT and T2DM were defined as glucose levels at 2 hours after glucose load between 7.8 and 11.0 or >11.0 mmol/l resp.

Results: there was no increase in plasma glucose and insulin levels or glucose AUC during 2 years of GH. Insulin AUC (30.2 to 38.6, p=0.047) and HOMA-IR (1.2 to 1.8, p=0.03) increased significantly during 2 years of GH. Since fasting glucose tended to be correlated with age and fasting insulin was correlated with BMI, results were corrected for age, sex and BMI. IGT was present in 8/42 after 2 years of GH, while not one patient developed T2DM.

Conclusions: 2 years of continuous GH treatment in young adults with Prader-Willi syndrome, who have been treated with GH during childhood for several years, does not impair glucose homeostasis and does not lead to T2DM.

POSTER #12 GROWTH HORMONE TREATMENT IN ADULTS WITH PRADER-WILLI SYNDROME HAS SUSTAINED POSITIVE EFFECTS ON BODY COMPOSITION

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Introduction: In children with Prader-Willi syndrome (PWS), the benefits of growth hormone (GH) treatment are well established. Several one year studies have shown that GH treatment is also beneficial for adults with PWS, improving body composition. However, little is known about the longer-term effects. The objective of this study is to investigate the effect on body composition after adult height (AH) attainment, of either continuation of GH for 2 years or restart of GH for 2 years after cessation for a median period of 1 year.

Methods: Open-label, prospective study in 53 young adults with PWS performed in a PWS Reference Center in the Netherlands. All young adults received at least 2 years of GH after attainment of AH in a standard dose of 0.33 mg/m2/day (≈0.035 mg/kg/day). A DXA scan was performed at baseline and at 1 and 2 years to assess fat mass percentage (FM%) SDS and Lean body mass (LBM) SDS.

Results: In 27 adults who continued GH, estimated mean (95% CI) FM% SDS did not change during 2 years of GH (2.1 (1.9 to 2.3) SDS at baseline vs. 2.2 (2.1 to 2.4) SDS after 2 years, p=0.19), neither did LBM SDS (-1.9 (-2.4 to -1.4) SDS vs. -1.8 (-2.3 to -1.5) SDS, p=0.70). In 26 adults who restarted GH, FM% SDS decreased significantly, from 2.2 (2.0 to 2.4) SDS to 1.9 (1.7 to 2.1) SDS, p<0.001, while total body LBM SDS increased significantly from -2.3 (-2.7 to -2.0) SDS to -1.9 (-2.2 to -1.5) SDS, p<0.001. There were no GH-related adverse events during the study.

Conclusions: Continuation of GH treatment for 2 years after AH attainment maintains the positive effects on body composition attained during childhood, while restart of GH after discontinuation for 1 year improves body composition. Thus, adults with PWS benefit from longer-term GH treatment.

POSTER #13 EFFECTS OF GROWTH HORMONE TREATMENT ON THYROID FUNCTION IN PEDIATRIC PATIENTS WITH PRADER-WILLI SYNDROME

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Introduction: It is unclear whether hypothyroidism is present in patients with Prader-Willi syndrome (PWS). This study aimed to clarify the state of the hypothalamic-pituitary-thyroid axis and the effects of growth hormone (GH) treatment on thyroid function in pediatric patients with PWS.

Methods: We retrospectively evaluated thyroid function in 51 patients with PWS before GH treatment using a thyroid-releasing hormone (TRH) stimulation test (29 males and 22 females; median age, 22 months). We also evaluated the effect of GH therapy on thyroid function by comparing serum fT3, fT4, and TSH levels at baseline, 1 year and 2 years after GH therapy.

Results: TSH, fT4, and fT3 levels were 2.28 (IQR; 1.19 to 3.61), 1.18 (IQR; 1.02 to 1.24), and 4.02 (IQR; 3.54 to 4.40), respectively. In 49 of 51 patients, the TSH response to TRH administration followed a typical pattern; in 2 patients (4.0%), the pattern suggested hypothalamic hypothyroidism (delayed TSH peak after TRH). TSH, fT4 and fT3 levels did not change significantly during 1 or 2 years after GH treatment.

Conclusions: The TSH response to TRH showed a normal pattern in most patients, and thyroid function did not change significantly during the 2 years after initiating of GH treatment.

POSTER #14 SCREENING FOR CENTRAL ADRENAL INSUFFICIENCY IN CHILDREN WITH PRADER-WILLI-SYNDROME (PWS) WITH SINGLE COLLECTION OF ACTH AND CORTISOL LEVELS

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Background: Many of PWS features are explained by hypothalamic dysfunction, therefore these individuals are at high risk for pituitary hormonal

deficiency. When the pituitary begins to fail, there is generally a specific sequential failure of pituitary hormones, starting with GH, continuing through LH and FSH deficiency, and culminating in loss of TSH and ACTH. A high prevalence (60%) of central adrenal insufficiency (CAI) however, has been reported in PWS using the metyrapone test. Many children, including infants have undergone stimulation testing to confirm or rule out CAI. Several studies however, using same test and other different testing methods including insulin tolerance test (ITT), low dose/high dose ACTH stimulation, glucagon stimulation tests have reported differing results with much lower rates of CAI ranging from 0 to 14% in PWS subjects. Previous study has shown that basal cortisol is closely correlated with adrenal response to stimulation.

Objectives: To asses single basal ACTH and Cortisol level as screening and prevent further stimulation testing for central adrenal insufficiency in children with PWS.

Methods: We studied 105 children (60 males and 45 females) with genetic diagnosis of PWS. Sixty eight (60 %) had deletion I and II, 24 (23%) UPD and 13 had only positive DNA Methylation testing. Plasma basal Cortisol and ACTH levels were collected between 7:30 and 8:00 am. All participants were 6 months to 9 years of age on GH treatment without illness or any other stressful condition during testing.

Results: All had normal morning Cortisol and ACTH level but 2 children, age 2 and 5 years with low and 4 y.o. male with increased cortisol level. These 3 children had normal ACTH level. Repeat sample after a week, revealed normal both Cortisol and ACTH level in all 3 children.

Conclusions: In this large number of children with PWS, we found no clinically significant cases of CAI after morning basal Cortisol and ACTH level, suggesting that CAI is rare in PWS. The true prevalence of CAI in the PWS population remains unclear and clinical assessment and diagnostic procedures to establish the need for replacement are still far from perfect. Screening with single morning Cortisol and ACTH, however could prevent further stimulation testing as well as unnecessary glucocorticoid replacement.

POSTER #15 CENTRAL PRECOCIOUS PUBERTY IN A BOY WITH PRADER-WILLI SYNDROME DURING GROWTH HORMONE REPLACEMENT THERAPY

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Introduction: Prader-Willi syndrome is a genetic disorder characterized by obesity, short statue, hypotonia and hypogonadism. Delayed or incomplete puberty are usually found in PWS, whereas central precocious puberty is very rare. This study aimed to report the case of a boy with PWS who was diagnosed with precocious puberty during growth hormone replacement therapy.

Methods: We retrospectively analyzed the genetics, clinical characteristics and laboratory findings of the boy.

Results: By the age of 4, the boy had mental retardation, epilepsy, characteristic face features, short statue with feeding difficulty in Neonate, and many clinical criteria of PWS diagnosis, which was confirmed by DNA methylation testμMS-MLPAμ. Therapy with recombinant human growth hormone (rhGH) replacement (0.1 IU/kg/day) was started. 2 years later, he performed increased testicular volume and growth velocity, high testosterone levels and advanced bone age. An ACTH test yielded a normal response and A GnRH test showed premature activation of the hypothalamic-pituitary-gonadal axis with pubertal gonadotropin and testosterone levels (gonadotropin-releasing hormone stimulated LH peak 20.51 IU/L, testosterone 3.32 nmol/L). Magnetic resonance imaging (MRI) of hypothalamic-pituitary region was normal.

Conclusions: In PWS, puberty is usually delayed and secondary sexual characteristics are almost always incomplete. True precocious puberty is very rare and only a few cases have been reported. Our patient fulfilled all diagnostic criteria for CPP. The rare manifestations of CPP in patients with PWS has been attributed to brain lesions. We hypothesize that our patient's precocious puberty resulted from abnormal brain discharge caused by epilepsy. Next step, we will treat the patient with gonadotropin-releasing hormone analog (GnRHa) and follow up his pubertal development.

III. GASTROINTESTINAL & NUTRITION

POSTER #16 NUTRITIONAL PHASES IN 25 CHILEAN PRADER-WILLI SYNDROME CHILDREN: CASE SERIES

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Introduction: Prader-Willi Syndrome (PWS) is the most common cause of genetic obese and hyperphagia is the key concept associated to this uncommon condition. Most pediatrician and dietitian are not aware of the nutritional phases of this syndrome. Hence, clinician suspicion could not be focused on a hypotonic undernourished infant with feeding difficulties or normal weight and regular feeding behavior toddler. The aim of this study was to reproduce the nutritional phases on a Chilean serial cases.

Methods: A cross sectional study of 25 children with PWS on nutritional control at Clinica Santa Maria, Santiago de Chile during 2017-2018 was done. Nutritional status assessment was made according World Health Organization references. The classification on nutritional phases was made by clinical history using Miller and cols criteria.

Results: 25 children from infants to adolescents were assessed. 24% were under 2 years old and all of them were on I phase and all of them were underweight, risk or normal weight. Among 2 to 5 years old children 75% were at phase 1b or 2a and 66% of the children were normal weight. Over 5 years old subgroup 71% were on 2b or 3 phase and the same percentage were overweight or obese.When performing Fisher statistical test was obtained a significant association between age and nutritional phases but not between age a nutritional status.

Conclusions: In our Chilean series there was a correla-tion between age and nutritional phases that could be helpful to convey to clinician implicated on the diagnosis.

POSTER #17 REFLEXIVE EXPLORATION OF CHILDREN WITH PRADER-WILLI SYNDROME EATING HABITS

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Introduction: In Prader-Willi syndrome (PWS), eating disorders remain a major difficulty throughout their development. In the medical literature, the dietary problems/eating disorders of children and adolescents with PWS are addressed through four focal length: (1) nutritional phases (from feeding difficulties to hyperphagia); (2) eating behaviour, (3) pathophysiological aspects and (4) hormonal regulation. Thus, eating food habits have not been studied in terms of social determinants. That include the acquisition of social norms related to eating practices and table manners, food categories, neophobia behaviours and family interactions. In addition, available data are mainly obtained through the answers of parents or Carrers and not by a direct experimental observation.

Methods: The objective of this research program is to understand the eating practices of children aged 3rd to 18th in a "natural situation" by using an innovative method. Observations of family meals (n=15) will be carried out on the Ovalie platform, a modular observation platform - which in the case of this experiment will be used as a family dining room - equipped with data collection devices (cameras, directional microphones) controlled from a control room and backed by data collection and processing software (Emotion Facial Recognition, Social Interactions). The protocol will allow to replicate the context of family mealtimes by recreating conditions to those of the family. These filmed moments will be the subject of a "post-meal" reflexive screening and a double analysis: on the one hand, by the researchers to try to identify behavioural regularities and, on the other hand, by the individuals themselves, to explain their practices, based on collective reflexive interviews with family members.

Results: This innovative method allow to do a reflexive ethnography of the eating habits of children and adolescents with PWS in life contexts. The technical mechanism will be mobilized to study the influence of social and physical contexts on eating food habits. It will also allow facial recognition of taste emotions. By varying the social, family and cultural dimensions of the study population, this research will reveal the characteristics of eating practices considered socially "problematic". We will focus our analysis on the learning that takes place in a context of family consumption: table manners, body management at the table, social interactions. We will also study how parents regulate (obligation, negotiation or abandonment of social rules) these moments of collective mealtime.

Conclusions: The use of the Ovalie platform is part of a useful interscience approach to better describe, understand and explain food practices specific or not to PWS. The work carried out will lead to proposals for concrete applications in terms of therapeutic education, services in the field of living environment and food in particular. Special thanks to the Prader-Willi France association for funding this study

POSTER #18 ADOLESCENCE AND EARLY ADULTHOOD ARE CRITICAL TIMES FOR WEIGHT GAIN IN PEOPLE WITH PWS

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Background: It is well established that late adolescence and early adulthood are critical times in the development of the behaviours and consequences associated with Prader Willi Syndrome(PWS). It has been reported that without appropriate structures in place from a young age, poor behaviours and lifestyle have the potential to impact not only on the people living with or supporting the affected individual but the person themselves.Based on the estimated prevalence of PWS occurring of 1 in 15000-20000 live births there could be between 377 and 502 people with PWS in the state of New South Wales (NSW) Australia. In NSW there are limited options for help with management of people with PWS. One tertiary hospital childhood service only sees patients to the age of 12 while the other will see them to 18. Ours is the only clinic that manages patients with PWS after discharge from paediatric services. Transition to High School at 11-12 years of age and leaving High School (18-19 years of age) are often times of uncertainty and much change with the potential of greater access to food sources and money. It is also when young people with PWS want to seek more independence, which is particularly challenging for those afflicted with disease. This study aimed to look at whether age of referral into this clinical service made a difference to the weight progression over the following 10 years.

Methods: A retrospective analysis was conducted on patients who had attended the Royal Prince Alfred Hospital (RPAH) PWS clinic between 1991 and June 2019. Weight and waist were measured at each clinic visit. The cohort was divided into 2 specific age groups: age > 18 (Adult) on entry (post school) and < 18 (Adolescent, school attenders). Percent weight change was determined for the following 10 years where data was available. Analysis was conducted using SPSS Version 18.

Results: 110 people with PWS have attended the clinic since its inception. There was data on 96 of the patients. 47% (n=45, 53% female) of patients first presented as adults and 53% (n=51, 45% female) were first assessed in adolescence. The mean age of the Adult group was 27.02 + 8.5 yr, and the Adolescent group was 14.7 + 2.1 years ($p < 0.001$). The Adult group weighed more 97.9 + 26.1kg vs 81.3 + 27.8kg ($p<0.01$) and had larger waist circumferences 111.2 + 18.5cm vs 101.8 + 19.3cm ($p < 0.05$) on entry to the clinic. However the Adolescent group gained a greater percentage of weight at each year after entry for the 10 years analysed ($P<0.05$).

Discussion: This analysis shows that late adolescence to early adulthood can be a critical time for weight gain. This is thought to occur because of increased socialisation, greater burden of care and increased food access during this period.

Conclusion: Late adolescence and early adulthood is a critical time and more interventions are needed to help with the management of people with PWS through this period.

POSTER #19 A REAL-WORLD ANALYSIS OF WEIGHT CHANGE IN ADOLESCENTS AND ADULTS WITH PWS

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Introduction: Knowledge of how weight changes over time in the PWS population is important for understanding the contemporary natural history of the disorder as well as for assessing the impact of new treatments for hyperphagia.

Methods: We developed a text message-based, prospective cohort study of adolescents (12+) and adults with PWS to assess changes in weight and BMI over a six-month period in the 'real world' setting. Data was collected using a clinical mobile technology platform, and included gender, age, height and growth hormone (GH) therapy status at baseline. Weight was collected weekly while changes in height, living situation, access to food, activity level, and medication were collected at three-month intervals. For data analysis, repeated measures ANOVA and Cochran Mantel Haenzel tests were used for bivariate analysis, and generalized estimating equations were used for population-specific multivariable analysis.

Results: One hundred and sixty-five (165) individuals with PWS in the US and Canada enrolled

in the study, with a mean age of 19.7 years old (range 12 - 48). Thirty-three percent of the individuals were normal weight, while 15% were overweight and 52% were obese. The majority of adolescents were currently on growth hormone replacement therapy (78%) whereas only 38% of adults (18+) were receiving growth hormone. There was considerable variability in weight across participants (weight range: 71.4 to 466 lbs), but most individuals maintained relatively stable weight (median change: +2.02%) and BMI (median change +1.03%) over the study period and changes in living situation, activity, food access, medication had limited impact. Multivariable analysis for weight as an outcome showed that time in the study (weight increases slightly over time), gender (females had lower weight than males), and percentage of life on GH therapy (weight decreases as percentage of life on GH increases) were statistically significant fixed effects. Percentage of life on GH therapy (BMI decreases as percentage of life on GH increases) was also a statistically significant fixed effect for BMI as an outcome.

Conclusions: Participants were highly compliant over the six months of this text-based study, suggesting that a mobile technology-based data collection was readily accepted and highly manageable. We anticipate that the results of this study can inform future clinical trials for hyperphagia/obesity related therapies and provide a basis for understanding how well new therapies work in the real-world setting.

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POSTER #20 LACK OF RESPONSE TO DISGUSTING FOOD IN THE HYPOTHALAMUS AND RELATED STRUCTURES IN PRADER-WILLI SYNDROME

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Background: Prader-Willi syndrome (PWS) is a genetic neurodevelopmental disorder characterized among other symptoms by marked hyperphagia and food foraging even in garbage.

Objective: To investigate, based on a putative abnormal neural processing of disgusting signals, the brain response to visual representations of disgusting food in PWS using functional MRI (fMRI).

Methods: Twenty-one genetically-confirmed PWS patients, 30 age- and sex-matched and 28 BMI-matched control subjects viewed a movie depicting disgusting food-related scenes interspersed with scenes of appetizing food while fMRI was acquired. Brain activation maps were compared between groups and correlated with disgust and hunger ratings.

Results: At the cortical level, the response to disgusting food representations in PWS patients was qualitatively similar to that of control subjects, albeit less extensive, and engaged brain regions typically related to visually-evoked disgust, such as the anterior insula/frontal operculum, the lateral frontal cortex and visual areas. By contrast, activation was almost absent in limbic structures directly concerned with the regulation of instinctive behaviour robustly activated in control subjects, such as the hypothalamus, amygdala/hippocampus and periaqueductal gray.

Conclusions: Our study provides novel insights into the neural substrates of appetite control in a genetically-mediated cause of obesity. The presence of significant cortical changes further indicates that PWS patients consciously process disgusting stimuli, but the virtual absence of response in deep, limbic structures suggests that disgusting signals do not adequately reach the primary brain system for the appetite control.

IV. GENERAL MEDICAL ISSUES

POSTER #21 INCREASING PHYSICAL ACTIVITY IN ADULT PATIENTS WITH PRADER-WILLI SYNDROME: EFFECTIVENESS AND TRANSFERABILITY

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Introduction: Although physical activity (PA) is recognized as an essential component of the management of patients with Prader-Willi syndrome (PWS), most adult patients have insufficient level of PA. Day-to-day management of patients with PWS is particularly challenging and little is known about PA and sedentary patterns or the effect of PA interventions in these patients. The aims of this study were 1) to objectively quantify spontaneous PA and sedentary behavior using accelerometers in adults with PWS, 2) to evaluate the effectiveness and transferability of a home-based supervised exercise training program on habitual PA, physical function and body composition.

Methods: The study included adult women with PWS who received the PA intervention (PWS group) (NCT03673813). Subjects with PWS exercised at home, twice a week for 16 weeks, under the supervision of a specifically trained physical activity instructor. Each training session lasted one hour and was based on a combination of endurance and resistance training. In PWS group, body composition (DXA absorptiometry), physical activity (Actigraph accelerometers worn at the hip during 7 days outside of the exercise training program) and physical function (6- min walk test), were assessed before and after the PA intervention. Transferability of the program was assessed with the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework. Control women with common obesity matched on age and percent body fat (CON group) included in a study of our team (NCT01113996) were used for baseline comparison. They underwent the same assessments of body composition and habitual PA.

Results: Ten women with PWS (median [P25-P75] age: 29 years [24-33], body fat: 51.9 % [49.2-54.7] %) and 20 control women were included. Total physical activity was 37% lower in PWS group compared to

CON group (P<0.05). Sedentary time, especially in prolonged, uninterrupted sedentary bouts (≥ 30 min), was higher in PWS group. Participation to the exercise training program was excellent (median attendance: 32 [31-32] sessions). The program increased moderate-to-vigorous PA (+11 [13] min.d-1, P<0.05) and walking capacity (mean [SD]:+29 [37] m, P<0.05) but no effect was found on body composition or sedentary time.

Conclusions: Subjects with PWS are characterized by lower physical activity and more prolonged sedentary bouts. Supervised home-based exercise sessions are a feasible and effective strategy to improve physical activity and physical function in these patients, although body weight and body composition were not changed. This study shows the adjunct value of including a supervised PA intervention in the clinical management of adult patients with PWS.

POSTER #22 ICEBERG ALERT: SYSTEMATIC SCREENING REVEALS LARGE NUMBER OF UNDETECTED HEALTH PROBLEMS IN ADULTS WITH PRADER-WILLI SYNDROME

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Introduction: In Prader-Willi Syndrome (PWS), up to 3% of patients die every year. In half of the patients, the cause of death is of cardiovascular origin and / or obesity-related. Cardiovascular problems have a multifactorial origin, most of which relate to an excess of energy intake, compared to energy expenditure. On the one hand, excess energy intake due to overeating can cause morbid obesity, leading to diabetes and secondary cardiovascular complications. On the other hand, energy expenditure is low due to low muscle mass, which can further deteriorate due to undetected hormone deficiencies (like hypogonadism, hypothyroidism and GH deficiency). On top of this, fatigue (due to undetected hormone and vitamin deficiencies) can reduce exercise tolerance, thereby further increasing obesity. Due to the behavioral phenotype of PWS (patients do not report pain and hardly ever complain about physical problems), hormone deficiencies and other comorbidities often remain unnoticed. Undetected co-morbidity can lead to medical complications, requiring admission to the hospital ward or intensive care unit. Systematic screening can prevent part of the personal and financial burden of undetected comorbidity. In order to reveal yet undetected health problems, we performed a systematic health screening among adults with PWS.

Methods: We systematically screened 106 adults with PWS (mean age 31.3 ± 12.0 y) for the presence of (undetected) health problems. Based on a medical questionnaire, medical file search, extensive interview, thorough physical examination and biochemical measurements we made an overview of the health problems already diagnosed and those detected by our systematic screening.

Results: We found a striking number of undetected and untreated health problems and health risks. Undetected health problems (like hypogonadism, diabetes, hypothyroidism and hypertension) were present in 69% of the patients. 37% even had multiple undetected health problems at the same time. The most common health problems were hypogonadism (100% in males and 78% in females), vitamin D deficiency (51%) and scoliosis (44%). We also found many untreated health risks: 30% of the patients was not on a diet and 20% exercised less than 30 minutes a day.

Conclusion: We detected a striking number of untreated health problems and health risks among adults with PWS which, if left untreated, can pose a serious health threat. Systematic screening is needed to detect these problems in an early phase. This will prevent complications and might even reduce mortality in this vulnerable patient population.

POSTER #23 CAUSES OF DEATH IN PRADER-WILLI SYNDROME: LESSONS FROM 11 YEARS' EXPERIENCE OF A NATIONAL REFERENCE CENTER

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Introduction: In the last 20 years, substantial improvements have been made in the diagnosis, treatment, and management of patients with Prader-Willi syndrome (PWS). Few data on causes of death are available since those improvements were made. Our study described the causes of death among French patients with PWS over the first 11 years of experience of the nationwide French Reference Center for PWS (FRC-PWS).

Methods: The study population was patients with PWS who died in France between 2004 and 2014. Our study relied on two sources of mortality information at the national level: The French Epidemiological Centre for the Medical Causes of Death (CépiDc) Registry and the FRC-PWS database.Causes of death were classified into seven categories: respiratory, cardiovascular, gastrointestinal, severe infection, sudden/unexplained, other causes, and unknown. Descriptive statistics were calculated separately for children (<18 years) and adults (≥18 years).

Results: One hundred and four deaths were identified in France from 2004 to 2014. The median age at death was 30 years, ranging from less than 1 month to 58 years. Seventeen deaths occurred in patients under 18 years, with 70% of them in children under 2 years. Respiratory causes accounted for more than 50% of the deaths in patients with PWS. Among adults, most of the deaths were triggered by a respiratory failure while the main cause of death was a respiratory infection among children. Both, cause and age of death did not significantly differ according to gender or genetic subtype. In those adult patients with data on obesity, 98% were reported to be obese. We found no significant difference in the causes of death in patients with and without GH treatment.

Conclusions: Patients with PWS die prematurely. The principal causes of death are respiratory-related for all ages and, in most adults secondary to the complications of obesity. Thus, obesity prevention and adequate management of respiratory problems are the two most important ways to lower the mortality rate in this population.

POSTER #24 EVOLUTION OF THE FRENCH DATABASE OF CHILDREN WITH PRADER-WILLI SYNDROME

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Introduction: The French Reference Centre (RC) for Prader-Willi Syndrome (PWS) labelled by the French Ministry of Health in 2004 began a national register of children with PWS in 2005. In 2008, a cohort study in the different competence centres has been implemented in order to create a national database (DB). This DB includes medical, socio-demographic and familial data of children and adolescents with PWS.

Methods: Since 2016, we decided to improve the DB by reviewing the different variables. We took the opportunity to develop a new DB on Access 2016. This new tool contains 414 variables that cover multiple domains: genetic diagnosis, familial data, pregnancy and neonatal period, auxological and biological measurements, comorbidities, treatments, reeducative care and education. The old data collected before 2016 (n=348 patients) were transferred into the new DB. Between January 2016 and June 2019, we collected new data in the different French centres.

Results: Among the 1372 patients identified by the RC, 534 children were included in the DB. The population is composed of 51.9% of boys and the median age is 9.94 years (0.46-17.99). 462 patients (86.5%) have complete genetic diagnosis: 54.1% paternal deletion, 42.4% maternal uniparental disomy 15, 1.5% imprinting defect and 1.9% other genetic forms such as translocations. Among the 250 patients with paternal deletion, 87 (35%) have a known genotype subtype: 25% type 1 (long) deletion; 69% type 2 (short) deletion; 5% atypical deletion. For the remaining 72 patients (13.5%), we only have abnormal methylation profile results. The age at diagnosis was available for 512 patients. 72.5% of them were diagnosed during the first month of life (0.1 to 1 month) and for infants born since 2014 this percentage increases to 80.8%. In 22.9%, diagnosis is made during the first year of life with a median age at diagnosis of 2 months.

95.9% of 507 patients (data available) were treated with growth hormone (GH). Children born before 2014 began GH treatment at the median age of 1.6 years (0.3 to 14.7 years, n=366) whereas children born during the five last years started at 11.3 months (n=107).

Conclusions: We have now a very large and complete database including 534 children. This DB covering different aspects of PWS clinical and social profiles could be a powerful tool for retrospective and prospective studies. The first analyses show that the median ages at diagnosis and at start of GH treatment, decreased over time. In addition to our register, we developed case report forms for newborns and deaths. In addition, a PWS biological bank has been started since 2016 and to date samples from 185 patients included in the database are available.Special thanks to Pfizer Laboratory and the French Prader-Willi Syndrome Association.

POSTER #25 DEPRIVATION AND OBESITY IN PATIENTS WITH PWS

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Introduction: The Toulouse center of the French Reference Centre for Prader-Willi Syndrome (PWS) labelled by the French Ministry of Health in 2004 identified 1372 patients, included 534 children in the database and regularly follow about 120 children with PWS per year most of them addressed from all over the country because of a severe phenotype. We want to understand the causes of the severe obesity we observed in this population and particularly the link between deprivation and obesity which has not been evaluated in this rare disease.

Methods: We used the 11 items EPICES questionnaire which evaluates the deprivation of the family and was validated in a large cohort of 197 389 persons. The higher the score, the more deprived the family is; a cutoff of 30 was used to define deprivation. We administered EPICES questionnaire to 147 families during hospitalization in our center and Dykens hyperphagia questionnaire (HQ) and HQ for clinical trials (HQ-CT) to 40 patients among them. BMI was collected in all the 147 patients

Results: EPICES score was obtained for 147 families and children were 51% male with a median age of 7 years ranging from 0.3 to 19. Prevalence of deprivation in the 147 families is 25.9% (N=38), lower than the French general population (35%). BMI expressed in Z-score was significantly higher in patients with deprivation than in patients without deprivation (0.3 vs 2.35 p<005 Mann-Whitney test). The prevalence of obesity (Z-score BMI >2) is significantly higher in patients with deprivation than in patients without deprivation (50% vs 26.6%, p=0.015 Fischer test). Prevalence of deprivation is higher in patients with obesity (39.6%) than in lean patients (19%). HQ total score (20 vs 18), and HQ-CT score (5 vs 4) were not significantly different in patients without deprivation (N=35) vs patients with deprivation (N=5).

Conclusions: Deprivation is associated with higher prevalence of obesity in children with PWS albeit no difference on the severity of hyperphagia. These families deserve more attention and adequate follow-up.

POSTER #26 APPLICATION OF THE EVALUACIÓN INTEGRAL IDEAL® IN A CASE OF PRADER-WILLI SYNDROME: A PROPOSAL BASED ON THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH (ICF)

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Introduction: Children with PWS exhibit various clinical manifestations from the fetal and neonatal period that predispose them to neurodevelopmental, cognitive, physical and behavioral disorders. Our study propose the application of the Evaluación

Integral IDEAL® in the case of a child diagnosed with PWS, which is a comprehensive assessment based on the International Classification of Functioning, Health and Disability -ICF-, that works as an interdisciplinary tool that assess, identifies and describes changes in the components of a person's functioning, in order to guide the professionals, user and their family to take concerted decisions regarding the necessary actions that must be taken for its integral approach.

Method: Single case study, carried out with a 4-year-old boy with a confirmed diagnosis of Prader-Willi syndrome. The Evaluación Integral IDEAL® was implemented to assess the functions and body structures, activities and participation in the case studied, and its operating profile was also defined. The strengths and limitations of an assessment tool based on the ICF in a PWS case are analyzed from the professionals' perspective.

Results: The application of the Evaluación Integral IDEAL® allowed to identify clinical parameters of the current condition of the child, assess the status of functions and body structures, the performance of activities and participation according to age, and identify environmental factors that can influence their functioning and development. The functioning profile contributes to prioritize the attention needs, to define the goals of the comprehensive rehabilitation process and the intervention actions. Having an instrument with universal qualifiers, favors the interaction and communication of the rehabilitation team and the interdisciplinary for the approach and follow-up of people with Prader-Willi Syndrome, who require differentiated and multidisciplinary care.

Conclusions: The CIF it is reference framework to develop tools to measure or assess individual functioning, applicable to different contexts and populations. The application of the Evaluación Integral IDEAL® in the case under study allowed the identification of the variants of the children's functioning, beyond the medical diagnosis and the deficiencies. The assessment based on the realization of activities and participation, is key to guide intervention actions from different areas. The use of universal descriptors and qualifiers favor teamwork and communication between professionals and institutions. These findings allow us to consider that the Evaluación Integral IDEAL® is an alternative for the comprehensive approach of people diagnosed with Prader-Willi Syndrome, that are over 4 years of age. As it is an assessment tool based on the ICF, its application can be useful in clinical contexts and extend to other areas related to the rehabilitation of people with PWS.

POSTER #27 PRADER-WILLI SYNDROME. PRESENTATION OF A CLINICAL CASE

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Background: Prader-Willi syndrome is a genetic disease characterized by obesity with hypotonia and hypogenitalism and intellectual disability. With a frequency in general population 1 / 15,000 to 25,000 per live births. Most of them occur sporadically, where more than 70% of the cases are produced by deletions of paternal origin in the 15q11-q13 region, 28% of the cases by maternal uniparental disomies and less than 2% are caused by alterations of imprinting.

Objective: to describe the phenotypic characteristics of a sick adolescent with early diagnosis, adequate social and family stimulation.

Clinical case: male adolescent with 14 years obese, moderate intellectual disability, very small hands and feet, hypogenitalism, hypotonia that improved with rehabilitation and physical exercises carried out with his family, with adequate social relationship and multidisciplinary monitoring.

Conclusions: highlight the value of early diagnosis and the intervention of several specialists, allowing to provide genetic counseling to guide families. Achieving through several actions together improve the language, which the hypotonia disappears, reaching an adequate school and social incorporation, which elevates their quality of life.

POSTER #28 CARDIOVASCULAR AUTONOMIC REGULATION IN PRADER-WILLI SYNDROME

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Introduction: Patients with PWS have a higher cardiovascular (CV) risk but the underlying mechanisms are unclear – this may be favored by a dysfunction of the Autonomic Nervous System (ANS). However, data on CV regulation by ANS assessed by Heart Rate Variability (HRV) in PWS are inconsistent. In this study, we investigated HRV during sleep in a large cohort of young patients with PWS and in age-matched controls.

Methods: 57 children and adolescents aged from 1 to 18 years who underwent a polysomnography from September 2014 to January 2017 were included in this study: 37 patients with PWS (mean age 7.2 years, from 1.1 to 17.1, 18 female and 19 male) and 20 age-matched controls (mean age 8.5 years from 1.8 to 18.6, 11 female and 9 male). For patients with PWS, the genetic subtypes were a deletion in 20/37, a maternal disomy in 16/37 and 1 patient carried an imprinting defect. All patients were treated with growth hormone for a mean duration of 5.4 years. Sleep was monitored during a single night in the sleep unit (Natus equipment). Sleep stages, arousals and respiratory events were scored using standard criteria (AASM 2012). HRV was analyzed through Kubios software. We selected at least five minutes of ECG signal during each sleep stage. HRV was assessed both in time domain (SDNN, NN50 and RMSSD) and frequency domain (Energy in low frequency (LF: 0.04-0.15 Hz) and high frequency (HF: 0.15-0.40 Hz) bandwidths). The LF peak depend mainly on sympathetic components and HF peak reflects cardiac parasympathetic tone.

Results: The mean Heart Rate (HR) was significantly higher in PWS patients compared to controls in N2 and REM stages, and tended to be higher in N3 stage. Regarding time domain analysis, the RMSSD was significantly reduced in all sleep stages and the PNN50 was significantly reduced in N2 and REM stages, with a trend in N3 stage. Regarding the frequency domain analysis, a significant decrease in LF power during slow wave sleep was observed in PWS group compared to control group. HF power reflecting the parasympathetic tone was lower in PWS group but this trend was not significant.

Conclusion: This study showed an altered parasympathetic activity reflected by a reduction in pNN50 and RMSSD while HF power displayed a downward trend (p=0.06). This was also observed in dynamic evaluation of the ANS performed in patients with PWS aged more than 6 (18 of them were also included in the sleep study) (data not shown). For example, a reduced initial increase in HR with active standing (30/15 ratio) was observed in 9/19 patients (47%) compared to normal values. Our findings are in accordance with those of DiMario et al. (1994) who reported a decrease in HRV with deep breathing under parasympathetic influence. The decrease in LF power might reflect an associated decrease in sympathetic tone as shown by Purtell et al (2013) who reported a reduced LF HRV meal response in adults with PWS. These changes in ANS CV regulation may contribute to the increased cardiovascular risk in PWS. Additional studies are needed to further investigate the probably centrally mediated mechanisms.

POSTER #29 BEHAVIORS RELATED TO HYPERPHAGIA IN THE ARGENTINE POPULATION WITH PRADER WILLI SYNDROME: ASSOCIATION WITH THE TIME OF ATTENDANCE TO A TRANSDICIPLINARY TREATMENT

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Introduction: Nutritional aspects of individuals with Prader Willi Syndrome (PWS) involve diverse characteristics including abnormal satiety mechanisms, hyperphagia (uncontrolled appetite), and compulsive food behaviors. Hyperphagia has an early onset during childhood and is related to a persistent search for food, which greatly increases the risk of obesity. We aim to evaluate related behaviors to hyperphagia in individuals with PWS, and its relationship with time assistance to a transdisciplinary treatment.

Methods: This is an ongoing study of non-experimental, correlational, cross-sectional design. The sample, so far, is comprised by 27 individuals with PWS between 3 and 42 years old. Most individuals (89%) regularly attend a transdiciplinary-approach treatment at the SPINE Foundation. Nutritional approach includes safety measures to limit food access, an adequate nutritional plan for the patient, and nutritional re-education for both the family and patient. We asked the families to answer the hyperphagia questionnaire (HQ-CT). This questionnaire involves 9 questions, with Likert-type options ranging from 0 to 4 (thus ranging from 0 to 36) according to frequency of occurrence. Higher scores on HQ-CT are related to more hyperphagia-related behaviors. We obtained a license through the Foundation for Prader-Willi Research for the use of the questionnaire.

Results: In the present study the mean of hyperphagia score was 7.1±4.7, with ranging from 0 to 19. If we consider each individual item, the highest scores were found in the item that asked about steal or obtain food in secret (1.4±1.0). Furthermore we found a negative correlation between hyperphagia-related behaviors and time assistance to SPINE treatment (r= -0.502, p= 0.008).

Conclusions: Studing in detail hyperphagia-related behaviors in individuals with PWS is relevance to evaluate the eficacy of nutricional interventions. It also allow to identify possible critical points in the daily life of the patient, thus enabling improvements in the therapeutic approach. Our study demonstrated evidence of emerging efficacy related to a transdiciplinary-oriented approach towards the treatment of hyperphagia-related behaviors.

POSTER #30 CLINICAL PROFILE IN ADOLESCENTS AND ADULTS WITH PRADER WILLI SYNDROME

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Introduction: Prader Willi Syndrome is a rare disease neurodevelopmental disorder caused by the lack of expression of a 15q11q13 gene. Although clinical manifestations of this syndrome have been studied, there are no such descriptions in the Argentine population, and neither in patients undergoing transdiciplinary treatment. Previous descriptions include infantile hypotonia, poor suction, alterations in development, short stature, hypogonadism and hypogentaism, hyperphagia and excessive weight gain, cognitive and behavioral problems including tantrums, skin-picking among others. This study aim to describe the clinical profile of the population of Argentina with SPW that attends treatment to Fundación SPINE (SPINE).

Methods: This is an ongoing research, with a descriptive, cross-sectional, non-experimental design. Participants in the sample will be approximately 23 patients with PWS, without growth hormone therapy, who are treated for SPINE. They will be evaluated with the following studies: Ambulatory Monitoring Blood Pressure, Holter Cardiac, Polysomnogram (PSG), Hepato Biliary Pancreatic Ultrasound (BPH) Total Body Bone Densitometry (BMD).

Results: At the moment we are preparing database to realize later the statistical analysis. The objective is to identify: sleep disorders, detection of cardiac affections, body composition and detection of abdominal pathology.

Conclusions: One of the main conclusions that it is proposed to reach in this study is to identify if there are differences between the clinical profile of the Argentine population with PWS and the previous clinical descriptions. We consider it important to take into account the complementary studies to be able to evaluate in a more exhaustive way the population with SPW without growth hormone therapy. We believe it is necessary to develop a protocol for clinical studies for all patients with this pathology.

POSTER #31 NURSE EXPERIENCE WITH THE VENEPUNCTURE PROCESS OF ADULT PATIENTS WITH PRADER-WILLI SYNDROME

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Background: Prader-Willi syndrome (PWS) is a genetic neurodevelopmental disorder characterized by marked hyperphagia and morbid obesity, together with hormone deficiencies, abnormal behaviour in relation to food (obsessive thinking, food foraging, stealing, etc.). Veins in patients with PWS are difficult to find due to obesity and probably to generalised hypotonia including venous tone. Since treating a patient with PWS often requires the acquisition of blood samples, an experienced nurse is mandatory in the multidisciplinary team.

Objective: On the basis of our experience, we propose some recommendations to be taken into account for blood sample collection in adult patients with PWS.

Methods: Recommendations based on grade E of evidence

Results: The following items must be taken into account: Drink a lot of water the night before, come to hospital with clothes with warm long sleeves, use local heat with hot gel, gain her/his confidence, make her/him to be comfortable, use gloves and double tourniquet 5-10 cm above venipuncture site, use alcohol pads in order to dilate the veins, use butterfly as needles, put all the tubes to be filled near in order of priority, just in case you cannot get enough blood for all. If blood does not come out, put the arm below heart level or raise the forearm o turn the wrist so as to get more circulating blood. If you cannot get a good vein, then proceed to artery puncture (radial). Remember that they do not feel pain (high threshold) or if the patient is afraid of feeling pain, use lidocaine cream. Put an adhesive pressure strip. Use biohazard waste container. Finally, do not forget to draw and keep a map of good veins for every patient so as to check next time she/he comes.

Conclusions: Following a nurse protocol for blood collection and other care issues in adult patients with PWS is essential for the best achievement of clinical assays, investigational projects and also the routine clinical care.

POSTER #32 PATH FOR PWS STUDY: A NON-INTERVENTIONAL, OBSERVATIONAL, NATURAL HISTORY STUDY OF SERIOUS MEDICAL EVENTS IN PRADER-WILLI SYNDROME

▸ Lisa Matesevac[1], Jessica Bohonowych[1], Jaret Malloy[2], Tonya Haugen[2], Dongliang Zhuang[2], Elizabeth Roof[3], Elisabeth Dykens[3], Jennifer Miller[4], Shawn McCandless[5], Theresa Strong[1]

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Introduction/Background: The incidence of serious medical events in individuals with Prader-Willi syndrome (PWS) is largely unknown. The PATH (Paving the way for Advances in Treatments and Health) for PWS natural history study is being conducted to increase our understanding of the profile of medical events and behaviors associated with PWS, help contextualize observations in clinical trials, and aid in development of new therapies for treatment of PWS. PATH for PWS is sponsored by Zafgen, Inc. and the Foundation for Prader-Willi Research (FPWR) and is hosted by the National Organization of Rare Disorders (NORD).

Methods: This 4-year prospective longitudinal study was designed to advance understanding of medical history and events in participants with PWS. The primary objective is to identify the incidence of serious medical events (ie, any event resulting in death, is life-threatening, requires hospitalization or emergency room visit, or is medically significant) in participants with PWS. Additional objectives are to prospectively evaluate other medical outcomes, including the incidence of medical events of special interest (eg, non-serious thrombotic events), and prescription medication use associated with reported medical events. PWS-related questionnaires include the Hyperphagia Questionnaire for Clinical Trials, Food Safety Zone, PWS Profile, and Food Behavior Survey.

Results/Discussion: The study enrolled 700 volunteers ≥5 years of age in the United States, Canada, Australia, and New Zealand. Of these, 231 were 5-11 years of age 191 participants were 12-17 years and 278 participants were ≥18 years. A subset of participants (301 enrolled) provided a blood sample to measure D-dimer levels. A summary of study progress will be presented.

POSTER #33 MORBIDITY AND MORTALITY IN PRADER-WILLI SYNDROME: IMPLICATIONS FOR CLINICAL PRACTICE

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Introduction: Prader-Willi Syndrome is a complex genetic condition that manifests often with behavioural difficulties and physical morbidity in childhood. It is characterised by deregulated eating behaviour, hyperphagia and often mild to moderate intellectual impairment. There is a lack of international consensus on how to manage and treat patients with Prader-Willi Syndrome

Methods: A systematic review was carried out to examine the Medline, Cochrane, PsychINFO, CINAHL, Web of Science and Scopus databases for published material in the field of Prader-Willi Syndrome and hyperphagia. We were interested in any published morbidity and mortality data related to the hyperphagia phenomenon in PWS.

Results: Our systematic literature search resulted in 1384 papers identified as significant to the topic. The abstracts from these papers were reviewed by two independent reviewers, and 270 were judged to meet our inclusion criteria. Of these papers 243 were evaluated by their full text. Morbid obesity, type 2 diabetes mellitus, obstructive sleep apnoea, respiratory failure and hypertension were all regularly listed as significant problems in the literature reviewed. A number of papers also listed more unusual sequelae secondary to the hyperphagia phenomenon in PWS, such as choking or gastric dilatation and perforation. There is a high mortality rate, with one study finding a mean age of death of 29.5+/- 16 years*.

Conclusions: Prader Willi syndrome is highly associated with increased obesity and associated morbidity related to this. Understanding the risks involved informs management decisions. More research would also benefit the management of Prader-Willi Syndrome and improve our understanding of its associated morbidity and mortality. *Butler MG, Manzardo AM, Heinemann J, Loker C, Loker J. Causes of death in Prader-Willi syndrome: Prader-Willi Syndrome Association (USA) 40-year mortality survey. Genet Med. 2017;19(6):635–642. doi:10.1038/gim.2016.178.

POSTER #34 PRADER-WILLI SYNDROME AND HYPERPHAGIA: WHAT IS KNOWN ABOUT TREATMENT AND PREVENTION?

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Introduction: Prader-Willi Syndrome is a rare and complex genetic condition that often manifests with a wide range of behavioural problems and learning difficulties in childhood. Patients are especially prone to excessive overeating, as well as food hoarding and stealing phenomena. It is a multifaceted and challenging syndrome to manage and there is a lack of international consensus as to how to manage hyperphagia in PWS.

Methods: Our review examined the Medline, Cochrane, PsychINFO, CINAHL, Web of Science and Scopus databases looking for published material in the field of Prader-Willi Syndrome and hyperphagia. We were interested in any published management strategies related to the hyperphagia phenomenon in PWS.

Results: Our systematic literature search resulted in 1384 papers identified as significant to the topic. The abstracts from these papers were reviewed by two independent reviewers, and 270 were judged to meet our inclusion criteria. Of these papers 243 were evaluated by their full text. Several different management strategies featured in our review, but we could broadly group them into three main categories: 1) medication including psychiatric treatments and endocrine treatments, 2) surgical intervention and 3) specialised MDT programmes, combining a calorie restricted diet with exercise and activities, often in a residential setting.

Conclusions: An MDT approach was frequently utilised in this complex syndrome with success. Residential programmes were also broadly successful in managing hyperphagia and weight gain in the syndrome, however the ethical questions around these still remain pertinent. More research would be beneficial to this evolving field of study and better help to inform management.

POSTER #35 IMPROVING CARE OF PRADER-WILLI SYNDROME: EVALUATION OF A NEW CARE PROGRAM COMBINING ADAPTED PHYSICAL ACTIVITY, NUTRITION AND THERAPEUTIC EDUCATION

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Introduction: Prader-Willi syndrome (PWS) is a rare and complex genetic disease characterized by hypothalamic-pituitary axis dysfunction combining eating disorders associated with hyperphagia and satiety deficiency, mild intellectual deficit and behavioral disorders. This disease requires continuous management through specific therapeutic education to prevent metabolic and cardiorespiratory complications related to obesity. Physical activity must therefore be regular, adapted to the disability, taking into account cognitive deficits and behavioral disorders. The presented study aimed to evaluate an innovative and individualized care program combining Physical activity, Nutrition and therapeutic education for adults with PWS who have been admitted to our hospital for 1 month.

Methods: Twenty-one adults PWS patients,16 females and 8 males (median age: 30.4 years [min 20.8-max 58.1]; median BMI 47.3 kg/m² [min 26.6-max 68.3]) admitted to our hospital were enrolled in this study. The program includes: 2 days of assessments allowing the medicine to prescribe a physical activity program adapted to the patient's phenotypic profile, based on indoor or pool sports or physiotherapy sessions. For 4 weeks, patients, in addition to their physical activity program, will benefit from group workshops on nutrition and physical activity, and meal simulations to assess eating behavior. After the 4-week program, patients are reassessed to measure their physical and functional abilities and metabolic parameters. The benefits of the program on eating behavior, observance of the program and on the weight curve is also measured.

Results: The results showed, after the program, an improvement in physical abilities (6-minute walk test: +9.5%) and respiratory parameters (+ 8%), an interesting weight loss (-3.7% of BMI) and a good observance of the physical activity program (90.5% of the patients). However, the eating behavior does not show any significant improvement with the evaluation grid used. It seems that this would require more group workshop sessions.

Conclusion: This study demonstrated that an innovative and individualized care program combining Physical activity, Nutrition and therapeutic education for adults with PWS can lead to significant improvement in various clinical and behavioral parameters. However, these preliminary results should be confirmed by a double-blind randomized study with a larger number of participants.

POSTER #36 TRANSLATIONAL RESEARCH TOOLS TO ACCELERATE THERAPEUTIC DEVELOPMENT FOR PWS

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Introduction: There are several challenges to the current therapeutic development pipeline for PWS. The fundamental genetic and pathophysiological mechanisms underlying PWS phenotypes and cellular phenotypes are unknown, making target identification difficult. The paucity of patients, the limited knowledge on the natural history of PWS, the lack of biomarkers and patient-centric outcome measures of treatment efficacy, the limitations related to the predictive validity of animal models - the extent to which the model predicts clinical efficacy - impede translational research and slow therapeutic development for PWS. In this context, the Foundation for Prader-Willi Research (FPWR) has developed several programs in collaboration with stakeholders from industry, academia and other patient organizations at the international level to overcome key barriers along the therapeutic development path for PWS.

Programs: I will discuss the goals, progress and achievements of the following programs:

1. The PWS iPSCs biobank was launched in 2018 thanks to the partnership between FPWR and the University of Connecticut-Wesleyan University Stem Cell Core to develop a centralized high-quality biobank of iPSC lines derived from individuals with PWS. These lines are available for academia and industry worldwide.
2. A partnership with the Autism Brain Network has been established in 2017 to streamline brain donation process for families, and enhance the collection and distribution of high-quality post-mortem tissue to researchers.
3. The PWS Pre-Clinical Animal Network was launched in 2016 to develop new models, validate pre-clinical mouse models of PWS and create a preclinical drug screening platform.
4. The International Consortium to Advance Clinical Trials for PWS composed of stakeholders from industry, academia, and patient organizations was established in 2015 to address clinical trial challenges for PWS. The consortium aims to develop outcome measures to assess treatment efficacy against hyperphagia and other behavioral challenges, and patient- and caregiver-focused benefit/risk assessment of new treatments.
5. The Global PWS Registry was developed in 2015 by FPWR in collaboration with international stakeholders in the PWS community to build a comprehensive clinical database to better understand the natural history and full spectrum of PWS characteristics, facilitate clinical trial recruitment and enrollment, and foster clinical research through the availability of de-identified and aggregated data to academic and industry collaborators.

Conclusion: Implementation of patient-centric, collaborative and international programs integrating the expertise of multiple stakeholders across the therapeutic development path are key to streamline, de-risk and accelerate therapeutic development for PWS.

Acknowledgements: I would like to thank the many contributors to these initiatives, including members of FPWR Research team, the PWS-Clinical Trial Consortium members, the PCAN members, the PWS Global Registry members, numerous individual scientists and clinicians who provided guidance, and all the patients and families who participated in many studies.

POSTER #37 PREVALENCE OF PRADER WILLI SYNDROME IN PINAR DEL RIO PROVINCE AFTER DNA METHYLATION ANALYSIS INTRODUCTION

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POSTER #38 PWS IN BRAZIL: FOLLOW-UP IN A REFERENCE CENTER

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Introduction: In 2015 we started our PWS specialized outpatient clinic. In 2016, after IPWSO Conference, a group of parents began the PWS Brazilian Association which allowed a better information access and care. Other activities are made to develop the knowledge of PWS in our country, like conferences and contact with pediatric societies. This resulted in precocious diagnosis and new PWS patients that came for our clinic.

Objective: To analyze SPW patient's follow-up characteristics in 2019 compared with 2015.

Method: The inclusion criteria were PWS patients that were followed in Instituto da Criança-HCFMUSP from 0-32 years old. We evaluated the age of diagnosis; genetic type of PWS; age of follow-up started, Z-Stature-SDS, Z-BMI-SDS and growth hormone treatment. All patients received orientation in diet (900 calories/day independent of weight), physical activity and behavior. Our team is composed by pediatric endocrinologists, dieticians, nurses; psychiatric, neurologist specialized in sleep disorders and otorhinolaryngologist.

R**esults:** We included 102 patients in 2019 (mean age:11.5±6.2y), and 51 patients in 2015 (mean age:10 ±6.5y). In 2019, 43% were deletion, 30,3% were maternal uniparental dissomy, 2,9% had imprinting defects and 22,5% had only positive methylation test.

The age of diagnosis decreased from 3,43±-3,28yto 2,8 ±3,3y, but the age of follow-up started was still high despite their reduction (4,95±4,26y to 4,5±4,1y). Also, we had a BMI improvement from 2,97 ±1,58SDS to +2,4 ±2,54SDS as in Z-Stature +1,41±1,52SDS to -1,22±1,33SDS. The incidence of obesity decreased from 72,9% for 60% in our patients. Regarding rhGH treatment, we had a great change. In 2015, only 29% of our patients were using growth hormone and this rises to 81,3% in 2019.

Conclusion: Our PWS specialized outpatient clinic could improve BMI-SDS and Z- Stature-SDS in a great number of patients. Indeed, more patients can have access to interdisciplinary team orientations and rhGH treatment. The precocious diagnosis and specially the start of a standard care were still important barriers for PWS in our hospital. The PWS association can help families to find information and refer for a specialized team.

POSTER #39 EPIDEMIOLOGICAL ASPECT OF SCOLIOSIS AND BONE MINERAL DENSITY IN TAIWANESE PATIENTS WITH PRADER-WILLI SYNDROME

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Introduction: Prader-Willi syndrome (PWS) is a genetic disorder that involves hyperphagia, obesity, hypogonadism, and short stature. The musculoskeletal manifestations includes laxity of ligaments, osteoporosis, and scoliosis. The purpose of this study is to assess the progression of scoliosis and bone mineral density of PWS patients in Taiwan

Methods: This was a retrospective study and chart review in which patients being diagnosed of PWS were recruited. Longitudinal follow-up of serial plain standing spine radiographs and dual energy X-ray absorptiometry (DEXA) were assessed.

Results: Thirty-four PWS patients, from 1 to 24 years of age, were collected, of which 16 patients were male and 18 patients were female. All patients were treated with growth hormone till the closure of epiphyseal plate. Thirty patients developed scoliosis (88%), in which two third had right major curve. Most of the deformities occurs at the thoracolumbar junction. For patients with scoliosis, the greatest Cobb's angle varied from 5 to 90 degrees with the mean angle of 18 degrees. Five patients (14.7%) had Cobb's angle more than 40 degrees. Only two patients received surgical treatment due to severe deformity. Interestingly, in our series, the severity of scoliosis is negative correlation with BMI.

The mean bone mineral density (BMD) in these patients increased as their age increased, from 0.545g/cm^2 at age of 2 to 1.043g/cm^2 at age of 23, but the Z-score seemed to decrease on the contrary, especially since their adolescence. The Z-score declined more rapid in females than in males.

Conclusions: PWS has several musculoskeletal manifestations during their lifetime, and scoliosis is one of the most frequently seen disorder. Although most of the cases do not need surgical correction, regular follow-up is still recommended since progression of the condition may occur. The Z-score of BMD decreased since their adolescence which implies the need for sex hormone replacement during these ages.

POSTER #40 CHARACTERIZATION OF PRADER-WILLI SYNDROME

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Introduction: Prader-Willi syndrome is a genetic disease characterized by hypotonia in childhood, hypogenitalism / hypogonadism, hyperphagia, obesity, variable intellectual disability.

Methods: four patients were studied are Prader-Willi syndrome, achieving clinical diagnosis, through the clinical or standard method.

Results: the four patients presented hypotonia in early childhood, retardation in psychomotor and language development. Obesity was presented as an infant, with a predilection of the trunk and avidity for food, hands and small feet, with short phalanges, hypogonadism improved with endocrinology treatment. The cognitive disability manifested in all patients was of a very variable degree.

Conclusions: the multidisciplinary monitoring of endocrines, physiatrists, speech therapists, defectologists and geneticists contribute to raising the quality of life of patients. Early specialized and family stimulation improves the school and social insertion of these patients.

V. GENERAL MEDICAL ISSUES INCLUDING ORTHOPAEDICS

POSTER #41 COMPARISON OF HIP AND KNEE ARTHROPLASTY RATES OF INDIVIDUALS WITH AND WITHOUT PRADER-WILLI SYNDROME

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Introduction: Prader-Willi syndrome (PWS) is a complex genetic condition, with a prevalence between 1:10,000 to 1:30,000. The prevalence of hip dysplasia in children with PWS is reportedly between 8% and 30%, but the consequences of their residual hip dysplasia is unknown. The purpose of this study was to comparatively estimate the number of total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures performed on adults with and without PWS, using a national hospital discharge database.

Methods: The National Inpatient Sample of the Healthcare Cost and Utilization Project is the largest all-payer inpatient care database, containing annual data from more than 7 million hospital stays; sampling weights and stratification variables are provided for producing estimates of more than 35 million hospitalizations nationwide. THA and TKA procedures were identified, then stratified by whether or not the patient had a diagnosis of PWS. The ages of the two groups and gender mix were compared, as was the length of stay for the procedure, and discharge status.

Results: From 2004 to 2014, 9.4 million patients nationwide, by weighted estimate, underwent THA (3.1 million) or TKA (6.3 million). Sixty-five patients were identified as having the diagnosis of PWS (39 with THA, 26 with TKA); seven patients per million having hip or knee arthroplasties had PWS. Sixty-eight percent of those with PWS were less than 50 years old, compared to only 7% of those without PWS ($p<0.001$). The female:male prevalence was 47:53 for patients with PWS and 60:40 for the total group. The mean length of stay was similar, but patients with PWS were more likely to be transferred to another facility after surgery (77% versus 36%, $p=0.008$).

Conclusions: Hip dysplasia prevalence is higher in persons with PWS, but the rate of late treatment with THA is much lower. We recommend active observation for the stable and improving hips, as the consequences of overtreatment of these children can be serious, including further delaying their neuromuscular development, or exposing them to possibly unnecessary peri-operative risks.

Level of Evidence: Nation-wide database analysis, Level III

POSTER #42 BONE MINERAL DENSITY DECREASE IN PATIENTS WITH PRADER–WILLI SYNDROME UNDERGOING GROWTH HORMONE THERAPY

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Introduction: Bone mineral density (BMD) is well known to decrease in adolescent and adult patients with Prader–Willi syndrome (PWS). Decreased BMD could be related to growth hormone (GH) deficiency and hypogonadism. Although studies have suggested that GH therapy improves BMD, we encountered some patients showing BMD reduction despite undergoing GH therapy. In the present study, we aimed to investigate the incidence of BMD decrease in PWS patients undergoing GH therapy from childhood to adolescent and whether there are sex differences in this reduction.

Methods and Results: Seventy patients (43 males and 27 females; age, 8–22.8 years; median age, 14.2 years) with PWS (deletion-type n=49, uniparental disomy-type, n=21) were examined. They had received, or were receiving GH therapy for >5 years (range, 5–14 years). We measured whole-body BMD by dual-energy X-ray absorptiometry, adjusting the BMD Z-score using patient height and age; patients with Cobb angle > 30° were excluded. Twenty patients [28.5%;15 males (34.9%) and 5 females (18.5%)] showed a marked BMD reduction (adjusted Z-score < -2.5 SD) during the observation period, while 19 patients [27.1%; 11 males (25.6%) and 8 females (29.6%)] showed decreased BMD (-2.5 SD< adjusted Z score<-1.5 SD). There was a significant negative correlation between age and adjusted BMD Z- score, which began to decrease in early childhood and became prominent at pubertal age in both the sexes. The tendency of reduction, however, was more pronounced in males than in females.

Conclusions: In patients with PWS undergoing GH therapy, the incidence of marked BMD decrease was higher in males than in females, suggesting that it may be related with gender difference in hypogonadism. Although GH therapy was not sufficient to improve BMD, the incidence of BMD marked decrease could be reduced by this treatment.

POSTER #43 POSTURAL ASSESSMENT OF THE SPINE AND LOWER LIMBS IN PEOPLE WITH PRADER WILLI SYNDROME

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Introduction: The present work aim to establish reference values of the different structural alterations of people with Prader Willi Syndrome (PWS), and to determine association between the severity of the spine deviations and the different imbalances that can be identified involving the lower limbs such as discrepancy of iliac crests and genu valgo.

Methods: We carried on a non-experimental, descriptive, cross-sectional study. All participants was evaluated with X-ray spinogram. The presence of scoliosis was determined and classified according to the region and affected areas, measured in degrees through Cobb angles. Using the same radiological study, the height difference of iliac crests was measured, drawing horizontal lines over each anterosuperior iliac spine, establishing the distance between both lines measured in millimeters. Furthermore, the extent of genu valgo was evaluated by means of the Morley classification, measuring the intra-malleolar distance in centimeters, and thereby reflecting the underlying severity. Spearman correlation coefficient was performed to assess correlations, and all statistical analyses were performed using SPSS software package.

Results: Main results showed valgus grade, acording to the Morley classification, 52% grade 2 (M = 4), 17% a grade 3 (M = 6.3), and a 30% grade 4 (M = 9.5). On the other hand 44% of patients had mild scoliosis (mean difference 9.2 mm), 6% had mixed mild / moderate scolisis (mean difference of 20 mm), 31% had moderate scoliosis (mean difference 4.7 mm), 6.2% with mixed scoliosis (mean difference 5.5mm), and 6.2% with a severe grade (mean difference 12mm).

Within grade 2 genu valgo, 20% had mild scoliosis, 7% mixed, 20% moderate, and 7% had severe scoliosis. Among patients with grade 3 genu valgo, only 7% had moderate scoliosis; whereas within patients with grade 4 genu valgo, 27% had mild scoliosis, 7% moderate, and 7% mixed. Finally, using Spearman correlation coefficients, we did not identify significant relationships between the different variables explored.

Conclusions: In this study, we did not identify relationships between the severity or degree of the variables explored, thus corroborating the idiopathic nature of scoliosis, but leaving a space of uncertainty in its relationship with the different postural disorders of the lower limbs. Although we did not obtain the expected results, evaluation of the motor and postural approach is important in subjects with PWS from early age, since despite the most common practice involves only the evaluation of the spine, different lower limb imbalances can be found in these patients, forgetting the essentials of motor development in the first years of life..

VI. CLINICAL TRIALS FOR HYPERPHAGIA AND BEHAVIOUR

POSTER #44 CHRONIC TREATMENT WITH LIVOLETIDE (AZP-531) DOES NOT AFFECT IGF-1 PLASMA LEVELS: PRECLINICAL AND CLINICAL RESULTS IN PEOPLE WITH PRADER-WILLI SYNDROME (PWS)

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Introduction/Background: Patients with Prader-Willi syndrome have increased circulating levels of the orexigenic hormone acylated ghrelin (AG) with a relative deficit of unacylated ghrelin (UAG). These abnormalities in AG and UAG levels are hypothesized to be involved in the underlying mechanisms of hyperphagia. UAG is a 28-aa peptide that does not bind the growth hormone (GH) secretagogue receptor and has intrinsic activities that can counteract some effects of AG. Therapy with livoletide, a first-in-class 8-aa peptide analogue of UAG, is hypothesized to functionally correct the relative UAG deficiency to improve hyperphagia in people with PWS. In addition to hyperphagia, PWS is also characterized by dysregulation of the GH/insulin-like growth factor I (IGF-1) axis. GH therapy in PWS improves short stature, body composition, physical strength, and cognition. The objective of these i nvestigations was to determine if livoletide affects levels of IGF-1 in rats and in people with PWS.

Methods: During a GLP 26-week toxicity study in 6-week-old rats, IGF-1 was measured (n=15/sex/group) on the last day of treatment with vehicle (VHL) and with livoletide at doses up to 45 mg/kg/day. Serum IGF-1 was also evaluated during a GLP rat juvenile toxicity study from post-natal day 21 to 86. IGF-1 was measured (n=16/sex/group) with VHL and with livoletide at doses up to 75 mg/kg/day. Tibia length and bone mineral density of the femur and lumbar vertebrae (L4-L6) were measured at the end of the treatment period in the VHL and 75 mg/kg/day livoletide group (n=10/sex/group). During a 14-day Phase 2a study, IGF-1 plasma levels were measured in 22 people with PWS (ages 13 to 46 years; 14M/8F) on day 1 and 14 of livoletide therapy (60 µg/kg/day). Six participants (4M/2F) were under GH treatment during the two-week treatment with livoletide.

Results/Discussion: In the 26-week study, livoletide treatment at dose levels up to 50-fold the highest intended human therapeutic dose did not affect the IGF-1 serum levels in either sex (M: 519.5±73.7 ng/mL VHL vs 513.6±75.6 ng/mL livoletide 45 mg/kg; F: 353.6±46.1 ng/mL VHL vs 338.5±60 ng/mL livoletide 45 mg/kg). In the rat juvenile study, 64 days of livoletide treatment also showed no effects on serum IGF-1 levels (M: 497.2±57.5 ng/mL VHL vs 520.1±79.6 ng/mL livoletide 75 mg/kg; F: 381.8±49.2 ng/mL VHL vs 388.6 ±71.8 ng/mL livoletide 75 mg/kg). Neither tibia length nor bone mineral density were affected by treatment with livoletide in the growing animals. In the Phase 2a study on day 1, PWS participants treated with GH (GHP) showed higher levels of IGF-1 when compared with non-GH treated participants (NGHP) (353.8± 129.7 ng/mL vs 162.2±59.6 ng/mL; p<0.005). After two weeks of treatment with livoletide, IGF-1 levels in both groups were unchanged compared with baseline (GHP: 341±164.3 vs 353.8±129.7 ng/mL; NGHP: 155.8±54.7 vs 162.2±59.6 ng/mL).

Conclusions: In both adult and juvenile rats, chronic treatment with livoletide does not affect circulating concentrations of IGF-1. Furthermore, a Phase 2a clinical trial showed no difference in circulating IGF-1 levels in people with PWS on GH therapy treated with livoletide for 2 weeks. These results strongly suggest that livoletide does not impact the effects of GH in people with PWS.

Funding source: Millendo Therapeutics provided funding support for this study.

POSTER #45 NONCLINICAL DEVELOPMENT OF LIVOLETIDE (AZP-531): A PEPTIDE ANALOGUE OF UNACYLATED GHRELIN FOR THE TREATMENT OF HYPERPHAGIA IN PRADER-WILLI SYNDROME

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Introduction / Background: Prader-Willi syndrome (PWS) is a rare, complex neurodevelopmental genetic disorder characterized by hyperphagia and abnormal food-related behaviors that contribute to severe morbidity and early mortality and to a significant burden on patients and caregivers. There are no approved treatments for hyperphagia in PWS. Patients with PWS have increased circulating levels of the orexigenic hormone acylated ghrelin (AG) with a relative deficit of unacylated ghrelin (UAG). These abnormalities in AG and UAG levels are hypothesized to be involved in the underlying mechanisms of hyperphagia.UAG is a 28-amino-acid peptide that does not bind the growth hormone secretagoguereceptor (GHSR), unlike AG. UAG has intrinsic central and peripheral effects that counteractthe effects of AG and are exerted through a GHSR-independent mechanism. Livoletide is acyclic 8-amino-acid analogue of UAG with improved plasma stability and pharmacokinetics that is being developed as a therapy for hyperphagia in people with PWS.

Methods: The objective of this nonclinical development program was to support the clinicaldevelopment of livoletide, which includes a pivotal Phase 2b/3 clinical trial in patients withPWS initiated in early 2019. The program was designed to outline the safety pharmacology and the chronic toxicologic and toxicokinetic profile, and to identify parameters for clinical monitoring of potential adverse effects. Genotoxicity, safety pharmacology, reproductive toxicity, and repeat-dose 13-week toxicology studies were all completed. In the in vivo studies, livoletide was administered subcutaneously consistent with the clinical route of delivery.

Results/Discussion: Livoletide was not found to be cytotoxic or genotoxic in these studies. Safety pharmacology studies indicated no treatment-related effects on major physiological systems. Results from preliminary embryo-fetal developmental toxicity studies in rat and rabbit indicate that livoletide at high multiples of the anticipated human exposure is not associated with

adverse maternal toxicity, embryo-fetal toxicity or teratogenic potential when administered throughout the period of organogenesis. Repeat-dose toxicity studies of up to 26 weeks in rats and 39 weeks in dogs demonstrate livoletide is very well-tolerated, with no evidence of systemic toxicity. Cumulative data from these studies suggest that livoletide has a favorable safety profile. The highest chronic doses tested were 45 mg/kg in rat and 30 mg/kg in dog and considered as the NOAELs. These dose levels provided AUC values of greater than 50-fold the intended clinical systemic exposure (~1200 ng·h/mL). No anti-livoletide antibodies were detected in any of the toxicology studies mentioned above.

Conclusions: These results demonstrated favorable long-term safety of livoletide in animal models and support the subcutaneous administration of the highest anticipated human clinical Phase 2b/3 study dose.

Funding source: Millendo Therapeutics provided funding support for this study.

POSTER #46 LIVOLETIDE (AZP-531), AN UNACYLATED GHRELIN ANALOGUE, IMPROVES HYPERPHAGIA AND FOOD-RELATED BEHAVIORS BOTH IN OBESE AND NON-OBESE PEOPLE WITH PRADER-WILLI SYNDROME

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Introduction/Background: Prader-Willi syn-drome (PWS) is a rare, complex neuro-developmental genetic disorder characterized by hyperphagia and abnormal food-related behaviors that contribute to severe morbidity and early mortality and to a significant burden on patients and caregivers. While a significant proportion of people with PWS is obese (BMI ≥ 30 kg/m2), hyperphagia is observed in both obese and non-obese people with PWS. There is currently no approved treatment for hyperphagia in PWS. People with PWS have increased circulating levels of the orexigenic hormone acylated ghrelin (AG) with a relative deficit of unacylated ghrelin (UAG), a hormone which counteracts many of AG's effects. Livoletide (AZP-531) is a first-in-class UAG analogue that was previously shown to significantly improve hyperphagia, food-related behaviors, and metabolic parameters, and to be well-tolerated in a Phase 2a trial. [Allas S et al. (2018) PLoS ONE 13(1): e0190849]. Here we present additional analyses that examine the effects of livoletide in obese versus non-obese people with hyperphagia in PWS.

Method: The Phase 2a trial was a randomized, double-blind, placebo-controlled study which included 47 people with PWS (23 in the livoletide group and 24 in the placebo group). Participants received a single daily subcutaneous injection of livoletide or placebo during a 2-week treatment period. The study population was characterized based on the body mass index (BMI) classification: BMI ≥ 30 kg/m2 (obese), BMI < 30 kg/m2 (non-obese). The effect of livoletide on hyperphagia and food-related behaviors was assessed by the change from baseline in the 9-item Hyperphagia Questionnaire (HQ).

Results/Discussion: There was a total of 34 obese and 13 non-obese participants in the study. As expected, baseline BMI, body weight (BW) and waist circumference (WC) were significantly higher in obese compared to non-obese PWS participants (BMI: 42.6 ± 6.0 vs 26.1 ± 2.8, BW: 103.5 ± 23.0 vs 68.5 ± 9.1 and WC: 118.3 ± 15.5 vs 91.8 ± 7.7, respectively, $p<0.0001$). There was no significant difference with respect to the male to female ratio and the deletion to non-deletion ratio between the 2 populations. Hyperphagia scores were similar at baseline between obese and non-obese participants (HQ score adjusted for 0 to 36 scale to reflect 9-item HQ-CT: 12.8 ± 7.0 vs 14.0 ± 7.8, $p=0.6083$, respectively). Fasting AG and UAG levels were lower in the obese vs. non-obese groups (AG: 93.6 ± 72.6 vs 122.1 ± 54.4, $p=0.0275$, UAG: 123.9 ± 87.2 vs 154.1 ± 62.6, $p=0.0219$, respectively). Livoletide-treated participants experienced similar improvements in hyperphagia and food-related behaviors as measured by the HQ whether they were obese or non-obese.

Conclusion: These results highlight the potential of livoletide for treating hyperphagia in both obese and non-obese people with PWS and hyperphagia. Livoletide is being investigated further in the ZEPHYR Phase 2b/3 trial, an ongoing pivotal study which will provide data on the long-term safety and efficacy of livoletide in the treatment of hyperphagia and food-related behaviors in people with PWS.

Funding source: Millendo Therapeutics provided funding support for this study.

VII. MENTAL HEALTH, BEHAVIOUR & COGNITION

POSTER #47 THERAPEUTIC APPROACH OF EMOTIONAL COMPETENCIES FOR CHILDREN WITH PRADER-WILLI SYNDROME: THE EMOT PROGRAMME

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Introduction: People with Prader Willi Syndrome (PWS) have great difficulties of social adaptation that could be explained by disturbances of emotional competencies (i.e. ability to use emotions daily). However, the lack of knowledge about the emotional functioning of PWS people - and even more about its development during childhood – makes their care more complex. A first study (related to a doctoral thesis work) showed that PWS children (aged from 5 to 10 years) presented a significant developmental delay in expression, identification, comprehension and regulation of emotions, which is not only due to intellectual disability. Based on these results, the objective is to present a new therapeutic intervention programme (EMOT programme) specifically designed to help PWS children improve their emotional competencies.

Method: Twenty-five French children with PWS aged 5 to 10 were included. Based on a therapeutic and integrative approach, the programme is implemented by one of the usual children's therapists for 6 weeks. The effect of the program is measured by analysing the evolution of children's emotional competencies between a pre-intervention assessment session and two post-intervention sessions (immediate and after 3 months).

Results: The results show that the EMOT programme allowed children who benefited from it to improve the majority of their emotional competencies, and thus reduce their developmental delay. We find that the beneficial effect decreases as the task becomes more complex and requires more cognitive, perceptual and linguistic skills.

Conclusions: This work sheds new light on the emotional functioning and development of PWS and shows the relevance of a focused intervention.

POSTER #48 SEXUAL ABUSE IN EXCHANGE FOR FOOD IN PRADER-WILLI SYNDROME

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Introduction: Hyperphagia leading to morbid obesity is the most striking feature of Prader Willi syndrome (PWS). It is well known that PWS individuals often try to obtain food by begging, lying, stealing, or breaking into locked cabinets. Sexual abuse is common among populations with intellectual disabilities. Inappropriate sexual behavior in exchange for food in PWS has not been previously described. The aim of the study was to report and characterize sexual abuse in exchange for food in individuals with PWS and offer recommendations for prevention.

Methods: Demographic and medical data was collected from the files of all individuals (18 females /18 males, ages 12-44years) with a genetically confirmed PWS who live in residential homes designated specifically for this syndrome. In these hostels, individuals are under continuous supervision by trained staff. The main caregiver was interviewed for histories of sexual behavior and abuse.

Results: Nine individuals (5F/4M) ages (21-40years) from our cohort (n = 36) were exposed to sexual abuse (6 heterosexual and 3 homosexual). In 7/9 cases food reward was used by the perpetrator in order to attract his victim, although not always actually given. Age at sexual abuse ranged from 11-30 years. One girl suffered from abuse at the age of 11 and at an older age offered intimate touching in exchange for food. Most of the individuals did not disclose the event and five continued to initiate inappropriate sexual activity in order to obtain food.

Conclusion: Besides the high risk for sexual abuse present in populations with intellectual-developmental disabilities, individuals with PWS are at an additional risk due to their food-seeking behaviors. We report that 25% of adolescents and adults in our hostels suffered from sexual abuse, most of them in exchange for food. This assessment is most probably an underestimation due to unknown or unreported cases. Special programs and guidelines for sexual security with specific adjustments for the PWS population are mandatory.

POSTER #49 IMPROVEMENT OF COGNITIVE DEVELOPMENT IN PRADER-WILLI SYNDROME PATIENTS WITH EARLY GH TREATMENT

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Introduction: Growth hormone therapy (GHT) in older patients with Prader-Willi syndrome (PWS) has demonstrated the benefit in growth hormone response, improvement in body composition, decline fat percentage, and increment lean body mass. However, studies for PWS infants receiving GHT are scarce, with an improvement in motor and cognitive development in addition to body composition has been reported. In this study, we wish to know if the early GHT in early infants with PWS also can have these benefits.

Methods: A retrospective case analysis for PWS patients who received GHT before 3 years of age from 4 medical centers was conducted. The dose of GHT was 0.035 mg/kg/day (0.5-1 mg/m2/day). Patient demographics, molecular diagnosis, age of GHT, dose of GHT, developmental quotient (DQ), growth before and after treatment were analyzed. Another 20 patients who received GHT later than 3 years of age were used as control.

Results: Total 32 cases were analyzed. Twenty cases were treated before 12 months old while 12 cases were treated during 12-36 months. The mean age of start treatment is 11.4±8.2 months old (range 0.73-35.1, median 10.3). The mean follow-up period is 15±34.8 years (range 0.22-119.58, median 4.13). Cognitive development (Cognitive DQ/FIQ) was 64.9±17.8 which was significant higher than the group treated greater later than 3 years old (48.0±8.7, $p<0.001$).

Conclusions: Early administration of GHT benefits cognitive development in PWS.

POSTER #50 APPLICATION OF PROJECTIVE TECHNIQUES FOR THE THERAPEUTIC APPROACH OF PATIENTS WITH PRADER WILLI SYNDROME

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Introduction: The objective of this work is to analyze the usefulness of graphic techniques (drawing) as a therapeutic tool to know characteristics in behavior, allow the expression of emotions and behaviors, which are difficult to explain and externalize verbally in people with Prader Willi Syndrome.

The behavioral phenotype of PWS is defined by characteristic pattern of behavior disorder, usually showing rigidity, irritability, labile emotions, impulsiveness, impatience, tendency to confrontation, fabrications, manipulations, tantrums, repetitive behaviors, obsessions/perseverance, lies, self-injury behaviors and anxiety. However, many of these patients find it difficult to express their thoughts, emotions and behaviors due to their inherent intellectual and language delay. In this sense, graphic techniques might be a favorable tool since they rely mainly on a graphic resource, offering significant information for the therapeutic approach.

Methods: This was a non-experimental, descriptive, cross-sectional study. The sample consisted of 25 patients with PWS between 10 and 41 years of age, 15 men and 10 women. All participants receive transdisciplinary treatment at the SPINE Foundation. The projective HTP (house-tree-person) and family techniques were used for the assessment of behavioral trends.

Results: According to the criteria, for the graphic evaluation, established by Emanuel Hammer, Max Pulver y Josep LLuis Font, the following graphic indicators corresponding to the behavioral phenotype were identified: mental rigidity, anxiety, difficulty in adequate externalization and identification of emotions, impulsiveness, aggressive features, poor social skills, need for support and interaction, dependence and lack of empowerment, misfit self-concept, obsessive features, compulsive behaviors.

Conclusions: Graphic tests are intended to evaluate the psychic structurestructure and behavior characteristics in people, and discover emotions or internal conflicts. Any response to a projective material is significant and is considered as an indication of the patient's personality.

In our study, we found that graphical techniques (HPT and Family) are evaluation instruments that can be applied in a population with a mild to moderate intellectual disability, since all the patients correctly understood the task and were able to carry out an adequate production for the evaluation.

It is noteworthy that these graphic techniques provide information in the therapeutic context that, often, works as an invitation to encourage the

patient to speak and think about their thoughts, emotions and behaviors. Taking into account that this population has communication difficulties, it provides significant information and reveals conflicts that enable a therapeutic approach and that, otherwise, might not arise. It is important to emphasize that they although also provide convenient information to work with the patient, diagnosis cannot be established upon their basis. Graphic tests can be used as a tool or complement for facilitate the patient means to elaborate their problems and concerns, but it is not advisable to use it them as a single tool for diagnosis.

POSTER #51 EFFECTIVENESS OF ARIPIPRAZOLE FOR THE TREATMENT OF PRADER WILLI SYNDROME

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Introduction: The behavioral phenotype of subjects with Prader Willi Syndrome (PWS) is characterized by tantrums, stubbornness, oppositional and manipulative behavior, obsessive-compulsive characteristics, emotional lability, aggression, low tolerance to frustration, impatience, impulsiveness, withdrawal, and difficulties in competencies social and interpersonal relationships. Regarding compliance with maturational standards, there is a delay in motor development, language and some degree of cognitive impairment. Psychiatric disorders are frequent in adults with PWS, especially psychosis. Atypical antipsychotic drugs have revolutionized the treatment of schizophrenia and related disorders; being aripiprazole among these. Previous studies suggested that aripiprazole might be a promising treatment of PWS patients with psychosis. However, the FDA has released a warning in this regard among patients at a higher risk of presenting impulse control disorder, who may have uncontrollable desire and behavior while taking aripiprazole. Therefore, the objective of this work was to explore the efficacy of the aripiprazole among patients with PWS who attend transdisciplinary treatment at the SPINE Foundation.

Methods: This is a non-experimental, descriptive, longitudinal design study. The study population comprised individuals with PWS who attend transdisciplinary treatment at the SPINE (Socio-Psycho-Immuno-Neuroendocrinology) Foundation. Final sample was composed of 11 people with PWS, between 10 and 40 years. Half of the patients had previous indication of Aripiprazole, and half of the sample received this pharmacological indication while they assisted to treatment at SPINE Foundation. Aripiprazole is an atypical antipsychotic of third generation that reduces the adverse effects on the metabolism. Most of the patient regularly attended to transdisciplinary treatment at the SPINE Socio-Psycho-Immuno-Neuroendocrinology Foundation.

Results: A total of 11 patients between 10 and 40 years who attend or have attended transdisciplinary treatment at the SPINE foundation, medicated with aripiprazole, showing lack of favorable therapeutic response to this antipsychotic. On the basis of the evaluation of the mental health department of the SPINE Foundation, pharmacological activation effects related to aripiprazole were registered in all patients. The typical behavioral phenotype of subjects with PWS including irritability, opposition, affective lability, impulsiveness, aggressiveness, and low tolerance to frustration, were significantly exacerbated upon treatment onset with aripiprazole. Patients who started at low dosage (1 to 1.5 mg/d) were more irritable, oppositional, labile, promoting crisis. When the dose was increased to 5 mg/d or higher (some patients received up to 20 or 30 mg/d), serious behavioral episodes were documented, including disorganization, aggressiveness, self-injury, impulsivity with behaviors that put the patient's life at risk and home outbreaks. We identified a direct relationship between the medication dose and adverse behaviors.

Conclusions: In this study, aripiprazole was related to exaggerated pharmacological activation effects in subjects with PWS. Further studies are required to confirm this hypothesis in order to improve and anticipate the therapeutic approach of subjects with PWS and their families. Undoubtedly, a transdisciplinary approach was of the utmost importance in order to be able to assess the behavioral aspects of these patients among the different disciplines involved.

POSTER #52 EXPRESSIVE AND RECEPTIVE LANGUAGE SKILLS IN PATIENTS WITH PRADER-WILLI SYNDROME THAT ASSIST TO A TRANSDISCIPLINARY TREATMENT IN SPINE FOUNDATION

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Introduction: Individuals with Prader Willi Syndrome (PWS) have specific characteristics such as muscular hypotonia, short height, hypogonadism, intellectual disability, psychomotor delay, behavioral and psychiatric difficulties. Regarding the difficulties related to speech and language manifestations, these individuals can show alterations in speech articulation, hyper or hyponasality, and limitations in receptive, expressive language and pragmatic abilities. We aim to describe the linguistic profile of people with PWS, in particular of expressive and receptive language, and its relationship with the verbal intelligence quotient (VIQ).

Methods: We carried on a non-experimental, descriptive, cross-sectional study. All participants regularly attended to a transdisciplinary treatment at the SPINE Foundation. The treatment consist on a comprehensive social-psicho-immuno-neuro-endocrinology approach. Clinical Evaluation of Language Fundamentals-4 (CELF-4) was used to assess linguistic profile involving semantic, morphology, syntactic and pragmatic aspects.

Results: The sample consisted on 12 individuals with SPW between 11 and 45 years old, without growth hormone therapy. Principals results showed a more favourable performance regarding word definitions (5.0±2.5), number repetition (4.5±3.5) and formulated sentences (3.8±2.0). On the other hand, a worse performance was found in understanding spoken paragraphs (2.4±4.5), recalling sentences (2.8±1.8) and word classes total (2.9±2.3). When evaluating the relationship between the CELF 4 subtests and VIQ, we only identified a significant relationship regarding the working memory subtest (r: 0.73, p= 0.01).

Conclusions: In this study, the language profile of patient with PWS showed a better performance on expressive language skills, compared to comprehensive skills. We also identified an association between the VIQ and working memory. Considering the complexity of these patients, It would be necessary for future studies to focus on pragmatic skills, speech, voice, and stomatognathic aspects.

Table 1. CELF-4 scores

CELF-4 subtest	Score (mean±SD)
Recalling sentences	2.83±1.8
Formulated sentences	3.83±2.1
Word Classes Receptive	2.67±2.6
Word Classes Expresive	3.58±2.3
Word Classes Total	2.92±2.3
Word definitions	5.09±2.5
Understanding spoken paragraphs	2.42±4.3
Number repetition total	4.5±3.6
Familiar sequences 1Y2	3.92±3.8

Table 2. Relationship between CELF-4 and the verbal intelligence quotient (VIQ).

Domain	Spearman's correlation (Rho)	p value
Core Language Score	0.38	0.25
Receptive Language	0.14	0.67
Expressive Language	0.01	0.99
Language content	0.39	0.23
Language memory	0.27	0.42
Working memory	0.73	0.01

POSTER #53 PSYCHOLOGICAL ADAPTATION AND MENTAL HEALTH IN MOTHERS OF PEOPLE WITH PRADER WILLI SYNDROME

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Introduction: People diagnosed with Prader Willi Syndrome (PWS) require special care that is psychically and emotionally demanding. Mothers are usually the main caregivers of their children, meaning they may present difficulties adapting to the new situation. Being a caregiver could also be a risk factor for their mental health. There are few studies that focus on the mothers of people diagnosed with a disease. This study aims to evaluate the psychological adaptation and mental health of mothers of people with PWS.

Methods: The study has a non-experimental quantitative design, with a descriptive and cross-sectional scope. The sample consisted of 23 mothers with children with SPW between 1 and 35 years of age. The protocol consisted of a sociodemographic data questionnaire, the Psychological Adaptation Scale (PAS) instrument, which values greater than 3 represent an adequate adaptation, and the Adult Self Report (ASR) questionnaire, which includes a total score of problems in the mental health.

Results: Mothers of people with PWS have an average of 49.86 (SD=25.13) in the mental health problems scale. Regarding the levels of psychological adaptation, the total levels were 4.16. Concerning the different dimensions that compose psychological adaptation, an average of 4.04 was obtained for effective coping; self-esteem with an average of 4.22; spiritual or existential well-being with an average of 4.01; and, finally, social integration with an average of 4.39.

Conclusions: The mental health of the mothers of people with PWS seems to be affected, presenting problem levels (M = 49.86) much higher than the Argentine adults of the general population (M = 40.83) and resembling more the clinical population (M = 55.60), that is, those adults who are starting a therapeutic process.

Regarding the psychological adaptation levels, results show high levels in all of its dimensions. In other words, despite the overload and stress that caring for people with PWS represents, mothers are able to adapt psychologically to the disease.

POSTER #54 PERSONALIZED LEARNING PROFILE IN PRADER WILLI SYNDROME

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Introduction: The present study aims to assess the usefulness of a self-designed tool to identify strengths and weaknesses of cognitive characteristics in people with Prader Willi Syndrome (PWS).

People with PWS are characterized by intellectual disabilities, learning disorders and behavioral problems, demanding specific therapeutic interventions throughout different stages of their lives. The extent of cognitive deficit can be variable, usually mild to moderate. The gold-standard for measure this are Wechsler scales of intelligence (Wais and Wisc III), however, most patient with PWS have very low scores in the scale because concrete thinking and poor interpretation of tasks. For this reason, we start developing an instrument that allows defining a personalized learning profile (PLP). This instrument is being tested in our patients to deepen knowledge regarding impairment of functions related to reading, writing, spatial temporal organization, management and recognition of emotions, visal-motor coordination and numerical calculation; regardless of age.

Methods: This was a non-experimental, descriptive, cross-sectional study. The sample comprised 21 individuals with PWS, males and female, between 10 to 40 years, who regularly attend transdisciplinary treatment at the SPINE Foundation. In order to identify strengths and weaknesses in the cognitive profile, participants were evaluated using the Wisc-III and Wais-III scales, as well as a novel instrument designed in our institution, for defining a personalized learning profile (PLP).

This PLP is obtained from a series of activities to evaluate time-spatial organization, writing, reading, numbering, quantity notions, visual-motor coordination, text comprehension, and recognition of emotions. Each activity is classified as accomplished, in process, or not achieved; and classified into levels (1-3), allowing the therapist to establish goals for treatment and measure progress in the patient.

Results: According to the results of the Wisc-III and Wais-III scales, 10 patients showed strengths in the verbal scale (VS) and 10 patients in the execution scale (ES), and only one case did not present variation between scales. Whereas according to the data obtained with PLP, most patients presented strengths in the recognition of letters, numbers, and basic spatial notions and weakness in the comprehension of texts, additions and subtractions of tens, hundreds without concrete support. Most patients were able to complete level 1, but only few cases managed to complete levels 2 and 3.

Conclusions: We found out in our study that Wechsler scales can be usefully complement with PLP. The main cognitive difficulties found comprised failure in the sequential processing of information, working memory, logical-mathematical reasoning, accepting or understanding a point of view different from theirs, auditory verbal processing, attention, concentration, writing and executive functions. While the main strengths identified involved long-term memory and perceptual organization. This mixed information would be very useful to design specific intervention strategies aimed at the rehabilitation of the impaired cognitive abilities.

POSTER #55 VISUAL-MOTOR INTEGRATION IN PRADER WILLI SYNDROME WITHOUT GROWTH HORMONE

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Introduction: The present work aims to describe visual motor integration characteristics in people with Prader Willi Syndrome (PWS) without growth hormone. Within the clinical characteristics that are relevant for Occupational Therapy approach, patient with PWS has deficiencies in vision, fine and gross motor coordination, psychomotor development, sensory integration and learning, as well as intellectual disability and hypotonia.

Methods: A total of 17 people with a diagnosis of PWS between 13 and 39 years old, 64.7% males and 35.3% females, participated in the study. Another 10 cases must have been excluded from the study due to the irregularity with which they attend to treatment at the SPINE foundation, due to the taking of growth hormone or due to comorbidity with an autism spectrum disorder. The Beery-Buktenica Developmental Test of Visual-Motor Integration test (Beery VMI) was used. It was administered individually the complete form of the test consisting of 3 subtests. This instrument was designed by its authors to identify significant difficulties in visual motor integration, visual perception and motor coordination.

Results: The Beery VMI results showed that all the participants are in the Very Low category in the Visual-motor Integration subscale and in the Motor Coordination subscale. In the Visual Perception subscale, better results are seen, 88.2% obtained a Very Low score, a 5.9% Low score and a 5.9% Average score. When analyzing the scores of each section, it is observed that the highest values were found in the area that evaluates Visual Perception (53.73 ± 13.56), revealing a lower score in the area of Motor Coordination (47.35 ± 6.13) and Visual-motor Integration (48.94 ± 7.94).

Conclusions: According to the results obtained through the Beery VMI test, we can conclude that people with PWS without growth hormone, both adolescents and adults, show a better performance in visual perception, even though they are below the expected results for their different ages. In terms of motor coordination, their scores are even lower, also interfering with the Visual-motor Integration, since motor coordination and visual perception are the skills that influence their visual-motor integration performance. It is argued that with a regular and specific intervention in visual motor integration,

patients with PWS could improve their test results. At a certain point they will also be able to maintain and not worsen such skills.

POSTER #56 IDENTIFYING RELEVANT REHABILITATION GOALS FOR COGNITIVE TRAINING IN ADULTS WITH PRADER-WILLI SYNDROME

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Introduction: Although focusing on patients' identified personal goals is essential during rehabilitation, it can be challenging to choose relevant and realistic goals in patients with cognitive impairment. In Prader-Willi Syndrome (PWS), metacognitive difficulties lead to a lack of awareness of patients regarding their cognitive deficits that impact the choice of relevant rehabilitation goals. A method for choosing and evaluating a rehabilitation effect on personalized goals is Goal Attainment Scaling (GAS). Our aim was to explore the feasibility of using GAS for goals related to planning difficulties in patients with PWS during rehabilitation training.

Methods: In order to identify patients' planning difficulties as part of the ETAPP study (Evaluation of a Therapeutic Aid of the Planning function in Prader-Willi Syndrome), we designed a multi-steps approach involving firstly the patient's primary caregivers who filled in the Dysexecutive Questionnaire from the Behavioural Assessment of the Dysexecutive Syndrome and the 6-Item version of the Disability Assessment for Dementia. These questionnaires provided a basis for a phone-interview by a psychologist with the patient's caregivers regarding planning difficulties and allowed to evaluate the patient's executive difficulties in his/her ecological context. A face-to-face interview was then conducted by an occupational therapist (OT) with the patient him/herself using the report of the phone-interview with caregivers to lead the discussion. Comparison of those two interviews provided information about differences in perceived difficulties and priorities between the patient or his/her caregivers, as well as an indication of the patient's insight of his/her difficulties. Following the interview of the OT with the patient, personalized goals were selected and transformed into GAS. Two external judges scored GAS quality on SMART criterion extended. After the final training session, GAS were rated by the OT that conducted the intervention and by the patient.

Results: All goals could be set within the activity and participation domains of the International Classification of Functioning Disability and Health. Most goals were related to learning new strategies or using devices/support (charts, diary...) and included for example organising holidays, preparing a suitcase, using diary for key events, laundry management, attending leisure activity. Quality of GAS was found to very good (mean = 2.75/3). Results indicated that relevant goals for patients with PWS can be far from what caregivers and rehabilitation staff think of important issues. This gap can be the origin of situations causing important frustration and a lack of motivation for the patient and could explain the weakness of efficiency of some rehabilitation training. Results also showed that 65.2% of the patients considered that they had achieved their rehabilitation goals (scores from 0 to +2) versus 43.4% according to OT.

Conclusions: Using GAS for goals related to planning difficulties in patients with PWS appeared to be feasible and useful to focus on patient's relevant goals during rehabilitation. Implication of patient's caregivers is also essential to explore difficulties in patient's ecological context and improve adaptation in their life.

POSTER #57 FEASIBILITY AND EFFECTIVENESS OF A METACOGNITIVE TRAINING OF PLANNING ABILITIES IN ADULTS WITH PRADER-WILLI SYNDROME

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Introduction: Deficits in executive functions and intellectual disability are well documented in Prader-Willi Syndrome (PWS) and result in daily life difficulties and poor personal autonomy of patients. Difficulties in planning are particularly disabling for everyday actions like being able to plan an appointment and be there on time, being able to take the bus independently... One of the purposes of cognitive rehabilitation is to target and minimize disabled functions in patients. In executive dysfunction, metacognitive strategies are recommended because of a step-by-step approach which simplifies learning. For example Goal Management Training (GMT) helps individuals to efficiently encode goals in order to achieve a task by learning a mental checklist routine to maintain focus on the task. The aim of this study is to explore the feasibility and the effectiveness of a metacognitive strategy training on daily life planning difficulties in adults with PWS.

Methods: The ETAPP program (Evaluation of a Therapeutic Aid of the Planning function in Prader-Willi Syndrome) is a composite cognitive rehabilitation method based on GMT and others metacognitive strategies (auto-regulation scripts, problem-orientation...), consisting in six sessions of rehabilitation. With a double-blinded two-group randomized controlled trial, we compared planning performance of patients undergoing the cognitive training focusing on planning with those of a control group receiving usual care. Because focusing rehabilitation on patients' identified personal goals improves motivation and therapeutic alliance, daily life planning difficulties were identified and transformed into measurable goals using Goal Attainment Scaling (GAS). The main outcome was the performance on the Modified Six Elements (MSET) subtest from the Behavioural Assessment of Dysexecutive Syndrome. Patients were also evaluated on three executive tasks to assess updating, shifting and inhibition. In order to monitor punctuality and anticipation of actions, patients had to complete between-session assignments throughout the study.

Results: Over the course of eighteen months, we included 27 participants in the experimental group and 26 in the control group during their stay in the French Reference Center for PWS in Hendaye (France). Results show improvement of performances in the MSET and the others measures but no difference between the two groups. Both groups showed improvement on personalized goals measured with GAS (62.5% vs. 68.1%).

Conclusions: Quantitative data do not allow us to conclude to an effect of the cognitive remediation on executive functions but more qualitative data remind us the importance of personalized goal in rehabilitation and the variability of performance regarding intellectual disability. Considering the small number of sessions imposed by the length of their stay in the rehabilitation unit, a second study of the ETAPP program should be considered to explore the benefit of a more intensive training.

POSTER #58 PRESENTATION OF THE PRACOM (PRADER WILLI COMMUNICATION) PROJECT

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Background: The Prader Willi Syndrome (PWS) is a rare and complex, genetic disease characterized by a slight intellectual delay to moderate with obesity problems and disorders behaviors that can impede social relationships. The incidence is 1 birth on 25 000. The different manifestations of the syndrome result in social and professional integration difficulties (only 4% of adults PW in France live alone). The insertion in the community or in helping families daily by labor and management is difficult due to very frequent behavior disorders, for example, more than 80% of patients SPW are tantrums. However, at the present time, reasons related to these disorders are unknown.

Relevance of the research: In view to the difficulties of patients both academic and professional, and the impact of the disorders on families and caregivers (stress, burden...), the identification of factors explaining these disorders would allow a better understanding of the syndrome as a whole and a better adaptation of the care. Furthermore, the proposal of new therapies is a major issue in this syndrome for which there is today no medical treatment.

Objectives: The PRACOM (PRAder Willi COM munication) project is to identify and characterize disorders emotional functioning including those related to anger and their consequences at the behavioral level, to situate them in their contexts environmental (frequency, cause, consequences on the well-being and parental, school or professional relationships) and propose innovative therapeutic avenues to improve these behavioral disorders.

Methods: Different questionnaires, neuro-psychological tests, cognitive tasks and structured interviews will be administered to 30 children and 30 adults with PWS, 30 children and 30 adults control (without pathology), their parents and care professionals caregivers. At the end of these assessments, 3 therapies will be proposed to some patients with behavioral disruption: 1) a psycho-social program of emotional regulation, 2) a program of transcranial stimulation for adults with PWS, and 3) a program of external stimulation of the vagus nerve for children with PWS.

Expected results: A better understanding of the factors related to temper tantrums will improve management of patients SPW into their families and institutions and new therapeutic avenues may be proposed according to the relevance of the effects observed and extended to pathologies and similar disorders.

POSTER #59 EVALUATION OF A SPECIALIST MENTAL HEALTH / BEHAVIOURAL SERVICE FOR YOUNG PEOPLE WITH PWS

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Introduction: Children and young people with PWS are susceptible to comorbid mental health and behavioural problems and benefit from an early intervention to reduce disruption in their family lives and educational placements. National and Specialist CAMHS Learning Disabilities team at the Maudsley Hospital in London provides specialist behavioural interventions for young people with PWS, behaviour management advice to their families and carers, and multiagency liaison with local services. The results demonstrate effectiveness of the interventions offered by the Learning Disability Team in prevention and management of behaviour disorders and mental health problems in children and young people with PWS.

Methods: A short answer questionnaire was sent to twenty-two families who attended the service over the past 5 years in order to understand the effectiveness of the provided interventions and improvements in parental knowledge and understanding of behaviour problems associated with PWS.

Results: Feedback from the satisfaction survey indicated that 85% of families felt that their understanding and management of PWS and the comorbid mental health and behavioural problems had improved and over 70% of the families would recommend the service. A matched-paired t-test of the outcome measure used by the service, Children's Global Assessment Scale, showed a significant increase in scores from referral to discharge suggesting an overall improvement in functioning.

Conclusions: The results demonstrate effectiveness of the interventions offered by the Learning Disability Team in prevention and management of behaviour disorders and mental health problems in children and young people with PWS.

POSTER #60 CLINICAL AND ELECTROPHYSIOLOGICAL MARKERS OF GENETIC HIGH-RISK FOR PSYCHOSIS IN PRADER-WILLI SYNDROME

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Introduction: PWS is a rare genetic disease with a characteristic physical and behavioural phenotype resulting from the lack of paternal expression of maternally imprinted genes at 15q11-q15. This mainly due to a paternal deletion of this region (delPWS) or a maternal uniparental disomy (mUPD). While People with PWS all share common symptoms, only those with the mUPD genetic sub-type are at very high risk for psychotic illness (up to 60% in adults with mUPD). This increased risk of developing psychosis in mUPD has been hypothesised to be due to the over-expression of maternally expressed genes, which many have the potential to disturb the GABA/glutamate equilibrium, that has been shown to account to psychotic symptoms. However, very little research has been conducted to explore this hypothesis.

We are undertaking a case controlled study investigating markers of genetic high risk for psychosis in PWS using clinical, electrophysiological (EEG), psychiatric, neuroimaging (MRS), and cognitive measures. This study will determinate whether these markers differ according genetic subtypes of PWS and/or the presence of psychopathology. If they do, they might explain mechanisms of psychosis in PWS. The results of a pilot study investigating feasibility and acceptability of the methodology and the findings from adults with PWS in the pilot study with different genetic types will be presented.

Methods: Participants with the two main genetic types of PWS and also typically developing age and gender matched sibling controls will come for 2 days to the research centre in Cambridge, UK. The relationships between age, genetic type, psychopathology and EEG and MRS measures will be explored. The study will be divided in 5 parts:

1. EEG assessment: Measures of P50 sensory gating, mismatch negativity (MMN), and subsequent P300 responses will be conducted.
2. Neuroimaging: volunteering participants will undergo a structural MRI followed by the acquisition of GABA levels in the ACC and the temporal lobe using MRS.
3. Cognitive assessments: IQ (WASI), processing speed (Trail-making test), working memory (subscales of the WAIS), and sensory processing (The Sensory Perception Quotient) will be measured.
4. Psychiatric assessments: measures of schizotypy (O-LIFE), prodromal symptoms of psychosis

(CAARMS), anxiety, and depression (Glasgow Depression Scale and Glasgow Anxiety Scale) will be conducted. A more general psychiatric screening using the MINI-PASSADD will also be conducted.

Conclusion: This study is a unique opportunity to investigate electrophysiological markers of psychosis, cognition and proxy measures of brain GABA metabolism in PWS. The long term aim is to identify potential causative mechanisms for psychosis and inform treatment.

POSTER #61 I AM BILINGUAL, I AM PROUD... AND I AM GOOD! CODE-SWITCHING AS A TOOL TO DETERMINE THE STATUS OF GRAMMATICAL GENDER IN THE GRAMMAR OF A PWS ENGLISH-SPANISH BILINGUAL

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Introduction: Relatively extensive research has been conducted on the intellectual disabilities, behavioural disturbances and cognitive capacities of individuals with PWS. This contrasts with the fact that their language development remains almost entirely unexplored and limited to the speech and voice characteristics and the narrative abilities in monolingual individuals. To overcome this scarcity, we have set a program intended to investigate the linguistic abilities of this population. In this study we have used code-switched structures to investigate how grammatical gender is represented in the mind of a 34 year old adult male English-dominant English-Spanish bilingual (Spanish is the Heritage language) with PWS. Previous research has shown that typically-developing (TD) Spanish-dominant English-Spanish bilinguals prefer gender-matching switched Determiner+Noun (concord) and Subject+Adjectival Predicate (agreement) structures, as (1a) versus (1b) over non-matching ones, as (2a) versus (2b), which means that these bilinguals abide by the so-called 'analogical criterion (AC)': they assign English Nouns the gender of their translation equivalent in Spanish. For their part, English-dominant English-Spanish bilinguals are less consistent with their preference for the AC, as their ratings for matching items and their supplying matching articles and adjectivsdepends on the type of structure and on the experimental task (Liceras et al. 2016; 2017).

Methods: In order to determine whether this English-Spanish bilingual with PWS behaved like English-dominant TD English-Spanish bilinguals he was administered an Acceptability Judgment Task (AJT) and a Sentence Completion Task (SCT). In the AJT he rated 12 switched concord and 12 switched agreement structures (conditions 1 and 2) on a Likert scale numbered from 1 to 4, 1 being very bad and 4 being excellent. Six items were masculine and 6 were feminine (3 items were matching and 3 were non-matching).

(1a) Concord SP-EN matching:
(elthe-masc sunsol-masc)

(1b) Agreement SP-EN matching:
(the buildingedificio-masc es rojored-masc)

(2a) Concord SP-EN non-matching:
(lathe-fem. sunsol-masc)

(2b) Agreement SP-EN non-matching:
(the buildingedificio-masc es rojared-fem.)

In the SCT, he had to complete code-switched sentences by writing the Spanish determiner (concord) in 20 items as in (3) or the Spanish colour adjective (Agreement) in 20 items as in (4).

(3) Concord: [(__el/la__ booklibro-M)]

(4) Agreement: [(the booklibro-M es rojo-M/ roja-F]

Results: In the AJT he exhibits a high degree of acceptance for both matching and non-matching structures, although he has a stronger preference for the concord and the agreement structures that abide by AC, as he gives a higher rating to the matching structures in (1) than to the non-matching ones in (2). In the SCT he systematically abided by the AC when producing the two types of structures, thus performing at ceiling in both concord and agreement, as TD Spanish-dominant bilinguals do (Valenzuela et al. 2012; Fernandez & Liceras, 2018).

Conclusions: The fact that our PWS participant performs at ceiling in SCT and prefers between matching to non-matching code-switched concord and agreement structures in the AJT evidences that the representation of the gender features in his mind mirrors that of the Spanish-dominant TD bilinguals, and is therefore consistent with the position that parents should be supported in their decision to provide bilingual input to their children with PWS, since in this case and even though he is not Spanish dominant, he behaves like one when dealing with gender representation and processing.

POSTER #62 APPLICATION OF PQIF FOR BEHAVIORAL MANAGEMENT IN PRADER-WILLI SYNDROME

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Introduction: Parent orientation programs are conducted in order to train parents to better manage their children's behaviors. However, although there are researches that aim to develop and evaluate the effectiveness of programs, there is a shortage of programs that are specialized in patients with psychiatric or developmental clinical diagnoses. Therefore, this study aimed to evaluate the application of the Family Interaction Quality Program (PQIF) to parents of children with Prader-Willi syndrome, including the adaptations necessary to address the specific characteristics of the syndrome.

Methods: The group had seven participants who were parents of children up to the age of eight years with Prader-Willi syndrome who were invited to participate during the medical consultation at the pediatric endocrinology clinic of the Hospital das Clínicas of São Paulo. There were nine weekly meetings lasting two hours each. The program includes a previous group meeting to present the proposal, signing a consent form and applying measurement instruments, which were also applied at the last meeting. They are: Questionnaire on Prader-Willi syndrome, Parental Styles Inventory (PSI), Functional evaluation of problem solving.

Results: The parental style score demonstrated an increase in the use of positive parental practices for 6 of the 7 participants, and better observation and discrimination of the behaviors themselves. In addition, it was possible to observe an expansion in the repertoire of behavioral analysis - own and their children - and of appropriate management - affectionate dialogue, presentation of clear, coherent and consistent rules and avoidance of punishment.

Conclusion: The results indicate that PQIF is an important tool to assist the parents of children, including in the context of special needs such as Prader Willi Syndrome, and the management of behaviors in order to promote quality in family interaction.

POSTER #63 INVESTIGATING THE ALLOCATION OF VISUAL ATTENTION TO SALIENT STIMULI IN INFANTS AND YOUNG CHILDREN WITH PRADER-WILLI SYNDROME

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Introduction: The characteristics of Prader-Willi syndrome (PWS) include food preoccupation, and impairments in social functioning. Difficulties develop throughout early childhood, becoming more evident in adolescence and adulthood. Specific difficulties lie in the recognising and processing of visual social cues and an inability to effectively interpret social situations. In addition, individuals with PWS develop an insatiable appetite, with young children with PWS reported as demonstrating difficulties in shifting attention away from food, which might further impact on social functioning. The present study aims to 1) investigate if the allocation of attention towards visually-salient stimuli; emotional stimuli, and food stimuli in infants and children with PWS, differs from chronologically and social developmentally-matched typically developing children and 2) examine if infants and children with PWS show an attentional bias toward food stimuli relative to equi-salient visual or emotional stimuli, compared to typically developing children. This study aims to produce research that contributes to the progression and development of early stage preventative treatments, and also inform the use and development of other therapeutic strategies, such as intranasal oxytocin and agents that act on the feeding pathways of the brain.

Methods: Three groups of children will participate in the study: 15 children with PWS (N=15) aged between 12 and 30 months, 15 age-matched typically-developing children and 15 social developmentally-matched typically-developing children. A preferential looking paradigm will be used to assess infants' relative attentional allocation toward salience-graded emotional, food and (perceptually-matched) visual object stimuli. We hypothesise that PWS children will be disproportionately biased towards food stimuli over neutral or emotional stimuli.

Established questionnaires, including the Communicative Development Inventory, and ASQ-SE will be employed to assess early social, emotional and language development. The Early Social Communication Scales will provide measures of individual differences in nonverbal communication skills, and allow us to social developmentally-match the PWS participants to typically-developing children. The Dykens et al. (2007) 13-item Hyperphagia Questionnaire will be administered to assess food interest in infants and children with PWS, and our Background Questionnaire will assess family background; pregnancy and delivery, dietary information, genetic diagnosis, and general health.

Results: To date, of the proposed 45 participants, 7 PWS infants and 9 typically-developing children have been assessed. I will present the findings from our measures of social development and the preferential looking paradigm, and discuss any group differences between PWS and typically-developing children. Presently, our data suggests that there may be differences in the allocation of visual attention to stimuli, as well as nonverbal communication skills, and language.

POSTER #64 IMPORTANCE OF EARLY STIMULATION AND FOLLOW UP OF NEURODEVELOPMENT IN PATIENTS WITH PRADER WILLI SYNDROME. OUR EXPERIENCE IN CARDENAS CITY.

▸ Dayris Laura Falcón Rodríguez[1], Jorge Pedro Rodríguez[2], Omaida Sabatier García[3], Maryela Landa Muñiz[4]

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Introduction: Prader Willi syndrome (PWS) is a rare genetic disease, characterized by anomalies of the hypothalamus-hypophysis axis. It presents with profound hypotonia, starting in the neonatal period, mainly the first two years of life, hyperphagia with high tendency to develop morbid obesity in childhood and adulthood, learning difficulties and grave behavioral and/or psychiatric disturbances.

Methods: an observational study was carried out to four children with signs of presumptive PWS that were admitted in their first month of life at the neurodevelopment clinic of Cardenas city with the aim to set guidelines for early diagnose and assessment, through a multidisciplinary approach by a professional team composed of Clinical Geneticist, Genetic Counselor, Neonatologist, Neuro-pediatrician and Physiotherapists, with the aim to set guidelines for the assessment and early diagnosis of conditions resembling PWS. Early stimulation of neuromotor skills was started in a joint effort with the family along with a systematic assessment of their neurodevelopmental stages.

Results: the four patients, showed a severe hypotonia in the neonatal stage and delay in their psychomotor functions. Care and follow up showed an evident improvement of the neuromotor and language skills following physiotherapy and phoniatric therapies. A higher involvement of the family was achieved, upgrading their knowledge and acceptance of the condition.

Conclusions: with early stimulation and multidisciplinary follow up of patients with PWS a noticeable improvement of their psychomotor development and quality of life.

POSTER #65 INFLUENCES OF SOCIAL COGNITION AND REWARD PROCESSING ON AUTISM SYMPTOMS IN PRADER-WILLI SYNDROME

▸ Louise Gallagher & Sarah-Marie Feighan

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Introduction: Prader-Willi Syndrome (PWS) is a neurogenetic syndrome caused by the loss of expression of paternally expressed genes from the paternally inherited copy of chr15q11-

13 (Bittel et al., 2005). PWS is characterised by the onset of hyperphagia in childhood leading to morbid obesity. Hyperphagia in PWS is considered to be due to an impaired satiety response and an increased reward value of food. Autism Spectrum disorder (ASD) symptoms, including atypical social cognition, are prevalent in PWS cases and intriguingly, appear to increase in PWS across childhood (Bennet et al., 2015). The social motivation theory of ASD proposes that social cognition impairments are largely driven by social motivational deficits (Chevallier et al., 2012). We hypothesise that the onset of hyperphagia may reduce the reward value of social stimuli and contribute to the relative increase of ASD symptoms seen in later childhood in PWS cases.

Methods: We will phenotype ASD symptoms and hyperphagic behaviour in individuals with

PWS (n=60, age 4-40y) and age matched controls. To test if reduced valence of social reward underpins ASD symptoms in PWS, we will characterise social cognition comprehensively using a battery of accessible and validated eye-tracking paradigms. To test the relationship between reward valence for social cognition and hyperphagia, we will compare reward processing for food stimuli; social stimuli; and non-food/non-social stimuli. A dynamic preferential looking paradigm will be used to investigate differences in attentional bias between PWS cases and controls in hungry and satiated conditions.

Results: Data collection for this study is on- going. We will present preliminary analysis from the initial recruitment phase of performance of PWS cases and controls on the eye-tracking batteries.

Conclusion: The results of this study will help us understand if reduced valence of social reward underpins ASD symptoms in PWS and if it is related to the onset of hyperphagia.

POSTER #66 TREATMENT EXPERIENCES OF MENTAL AND BEHAVIORAL DISORDERS IN OUTPATIENTS WITH PRADER-WILLI SYNDROME IN GERMANY

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Introduction: Prader-Willi Syndrome is a neurodevelopmental disorder with typical clinical manifestations. The most consistent manifestations include hypotonia and poos weight gain in infancy, hypogonadism, early childhood-onset hyperphagia and obesity. Especially during young adulthood behavioral problems and often psychiatric disturbances occur frequently. Mostly tantrums, temper outbursts in combination with self-harm and aggressive behavior lead to problems in everyday life. These situations consequently create the need or psychiatric consultation. Unfortunately most clinical guidelines do not match the psychiatric needs of patients with Prader-Willi Syndrome. Side effects and adverse effects occur more often when using psychiatric treatment guidelines established for patients without Prader-Willi Syndrome. Moreover a variety of medications with antipsychotics, antidepressants and anticonvulsive agents can be seen generating variable response and not only beneficial effects.

Methods: A psychiatric outpatient clinic was establishes at the Hannover Medical School in 2010 due to the need of psychiatric treatment of patients with Prader-Willi Syndrome. Since then we treated more than 120 patients ages 12 to 55 with Prader-Willi Syndrome, some living at home with their families, most of them living in specialized institutions. Due to the lack of clinical studies concerning the psychiatric treatment of patients with Prader-Willi Syndrome we started a retrospective study to rate and summarize the treatment of typical psychiatric symptoms in patients with Prader-Willi Syndrome.

Results: Results so far indicate that treatment with serotonin reuptake inhibitors (SSRIs) reduces frequency and intensity of temper outbursts and reduces daytime sleepiness. Obsessive-compulsive symptoms decreased in severity. Patients treated with SSRIs presented a more balanced mood, self-harming behavior decreased. Less inpatient treatment was necessary. No significant weight gain was reported but uneasiness and insomnia forced us to cease the medication in some cases. Overall side effects did not occur more often than in general psychiatric patients treated with SSRIs.

Conclusions: SSRIs represent a well-tolerated medication to treat the typical psychiatric symptoms frequently seen in patients with Prader-Willi Syndrome as listed above. As far as our experience goes, SSRIs can be seen as a first line medication in the psychopharmacological treatment of patients with Prader-Willi Syndrome.

PROFESSIONAL PROVIDERS' AND CAREGIVERS' CONFERENCE: PROGRAMME

THE CONFERENCE WILL BE HELD IN THE CHÉ GUEVARA ROOM

THURSDAY 14TH NOVEMBER

08.00 – 08.30: Registration

08.30 – 10.00: Session 1: Opening and overview about special provisions and services for PWS in different countries

08.30 – 08.45: Welcome, Opening and Greetings
Norbert Hödebeck-Stuntebeck, Chair of the Professional Providers and Caregivers Board of IPWSO, Diakonische Stiftung Wittekindshof and Prader-Willi Syndrome Institute Germany
Tony Holland, IPWSO President, University of Cambridge, UK Raiza Parés Ojeda, University of Ciego de Avila, Cuba

08.45 - 09.00: Overview Cuba. Raiza Parés Ojeda, University of Ciego de Avila, Cuba

09.00 – 09.15: Overview Australia. Craig Moore, Interaction, Australia and Neil Gumley, Service Manager, Melbourne, Australia

09.15 – 09.30: Overview Argentina. Jorgelina Stegmann, SPINE Foundation, Argentina

09.30 – 09.45: Overview Ireland. Laura Keane, Resilience Care, Ireland

09.45 – 10.00: Overview Japan. Yoshiro Kato, Kansai University of Welfare Sciences, Japan Takayuki Kido, "ikiiki" non-profit organisation, Japan Yasunobu Yamada, Residential Rehabilitation Institution "Teran Hiroba", Social Service Organisation "Doyukai", Japan

10.00 – 10.30: Break

10.30 – 12.00: Session 2: Early Intervention

10.30 – 10.35: Introduction
Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof , Germany

10.35 – 10.50: Main challenges in adults with PWS. Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof , Germany

10.50 – 11.15: Physical development. Constanze Lämmer, Children's Hospital St. Bernward, Germany

11.15 – 11.40: Cognitive, emotional, social development. Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof, Germany

11.40 – 12.00: Parents and Environment. Constanze Lämmer, Children's Hospital St. Bernward, Germany

12.00 – 13.00: Lunch

13.00 – 14.30: Session 3: PWS and Aging

13.00 – 13.30: Medical and cognitive aspects of aging. Larry Genstil, Genstil Institute of Human Behaviour, Israel

13.30 – 14.00: Emotional aspects of aging. Larry Genstil, Genstil Institute of Human Behaviour, Israel. Damien Jones, Interaction, Australia

14.00 – 14.30: Social aspects of aging. Damien Jones, Interaction, Australia

14.30 – 15.00: Break

15.00 – 17.00: Session 4: Handling crisis situations and challenging behaviour

15.00 – 15.10: Systemic view
Norbert Hödebeck-Stuntebeck , Diakonische Stiftung Wittekindshof, Germany

15.10 – 15.30: Legal basics and ethics
Tony Holland. University of Cambridge, UK

15.30 – 16.00: Prevention. Svetlana Labun, Regens Wagner Absberg, Germany
Norbert Hödebeck-Stuntebeck , Diakonische Stiftung Wittekindshof, Germany

16.00 – 16.30: Handling. Michael Pethe, Deputy Home Director, Switzerland

16.30 – 17.00: Reflection: Concrete support within a Rogerian practice framework
Christine Ford, Community Connections, New Zealand

FRIDAY 15TH NOVEMBER

08.00 – 08.30: Registration

08.30 – 10.00: Session 5: People with PWS at home - Family support

08.30 – 09.00: Basics for families
Marguerite Hughes, Vice-President, IPWSO

09.00 – 09.20: Model of a specialist mental health / behavioural service. Natasa Momcilovic, Maudsley Hospital, London, UK

09.20 – 09.40: Nutrition in a family environment. Constanze Lämmer, Children's Hospital St. Bernward, Germany

09.40 – 10.00: Physical exercise in a family environment. Georgina Loughnan, Prader-Willi Syndrome Clinic, Royal Prince Alfred Hospital, Australia

10.00 – 10.30: Break

10.30 – 11.15: Session 6: Teachers' world

10.30 – 11.15: Issues with teaching people with PWS in the classroom. Larry Genstil, Genstil Institute of Human Behaviour, Israel

11.15 – 12.00: Session 7: Neuropsychology in PWS

11.15 – 12.00: A Neuropsychological view of PWS. Hubert Soyer, Regens Wagner Absberg, Germany. Svetlana Labun, Regens Wagner Absberg, Germany

12.00 – 13.00: Lunch

12.30 – 13.00: Poster presentations

13.00 – 14.30: Session 8: Science and Research

13.00 – 13.30: Overview of PWS research themes. Tony Holland, University of Cambridge, UK

13.30 – 13.45: Current and planned future clinical trials. Nathalie Kayadjanian, Foundation for Prader-Willi Research, USA

13.45 – 14.00: Iceberg alert: systematic screening reveals large number of undetected health problems in adults with Prader-Willi syndrome. Laura de Graaff, Erasmus MC Rotterdam and Dutch Center of Reference for Prader-Willi Syndrome

14.00 – 14.15: Improving care of Prader-Willi syndrome: Evaluation of a new care program combining Adapted Physical Activity, Nutrition and Therapeutic Education. Virginie Laurier, Hôpital Marin Hendaye - AP-HP, Unité Prader–Willi, Hendaye, France

14.15 – 14.30: Project ECHO: transferring knowledge through case-based learning and telementoring. James O'Brien, Board member of IPWSO, Australia

14.30 – 15.0: Break

15.00 – 16.45: Session 9: New Developments

15.00 – 15.20: Standards - how to develop first ideas. Laura Keane, Resilience Care, Ireland

15.20 – 15.40: Developing summer camps for people with PWS. Michael Pethe, Deputy Home Director, Switzerland

15.40 – 16.00: Developments in PWS in Austria. Stefan Pimmingstorfer, Caritas für Menschen mit Behinderungen/ Caritas Upper Austria

16.00 – 16.20: Supporting health situations in Fejo, Denmark. Karin Birkedal, Bostedet Solvang ApS, Denmark. Trine Jensen, Bostedet Solvang ApS, Denmark. Christina Brydegaard, Bostedet Solvang ApS, Denmark

16.20 – 16.45: Transition – the role of the endocrine nurse. Maria Pedersen, Karolinska University Hospital, Sweden

16.45 – 17.00: Session 10: Summary and perspective. Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof

PROFESSIONAL PROVIDERS' AND CAREGIVERS' CONFERENCE: SPEAKERS

KARIN BIRKEDAL, BOSTEDET SOLVANG APS, DENMARK. *Karin@solvangfejoe.dk*

Founder and director of "Bostedet Solvang ApS" (C.O).

CHRISTINA BRYDEGAARD, BOSTEDET SOLVANG APS, DENMARK. *Christina@solvangfejoe.dk*

Trained Nurse – health profession at "Bostedet Solvang ApS".

LAURA DE GRAAFF, MD, PHD, ERASMUS MEDICAL CENTER, ROTTERDAM, THE NETHERLANDS. *l.degraaff@erasmusmc.nl*

Dr de Graaff leads the Center for Rare endocrine Genetic Syndromes at the department of Internal Medicine, Erasmus Medical Center in Rotterdam, the Netherlands. Apart from clinical research, Dr. de Graaff leads a fundamental research line investigating biomolecular pathways and cellular mechanisms involved in rare endocrine genetic syndromes. Dr de Graaff obtained her medical degree from the University of Leiden in 2001. She finished her PhD in 2008, based on genetic studies in patients with congenital hypothalamic and pituitary disorders. In 2015 she finished her medical training in Internal Medicine-Endocrinology and launched the Center for Rare endocrine Genetic Syndromes (CRGS). Its multidisciplinary team takes care of adults from five national reference centers which are part of ERN-ITHACA (Intellectual Disability and Congenital Malformations) resp. the Endo-ERN.

CHRISTINE FORD, COMMUNITY CONNECTIONS, NEW ZEALAND. *Christine.Ford@ccslt.org.nz*

Christine Ford has worked in the disability sector for approximately thirty years, specialising in support to adults and children who have complex needs and challenging behaviour. She has also worked as the manager of social work service to vulnerable children and as specialist clinician to people with disabilities who have engaged in harmful sexual behaviour. Christine is a New Zealand registered Social Worker. She holds a Bachelor of Arts degree (Sociology) with Postgraduate Diplomas in Disability Studies (Autism) and Social work/ Social Science. She currently works as the Behaviour Specialist for Community Connections: a supported living service based in the North Island of New Zealand.

LARRY GENSTIL, PHD, MEMBER OF PPCB, PSYCHOLOGIST OF THE PWS MULTI-DISCIPLINARY CLINIC AT SHA'ARE ZEDEK MEDICAL CENTER, JERUSALEM, ISRAEL, OWNER AND PROFESSIONAL DIRECTOR, GENSTIL HOSTEL FOR PEOPLE WITH PWS. *genstil@gmail.com*

Born in the US, Larry completed an MS and a Ph.D. at the University of Southern California in Los Angeles. He is a psychologist who was licensed in California and is currently licensed in IsraelHe moved to Israel after marrying an Israeli, and they have lived there since 1986. They have children and grandchildren.Larry began working with people with PWS in 1979 and has done so continuously since 1993. He runs a large group home in a suburb of Jerusalem for people with PWS. In addition, he is the psychologist of the Israeli Prader-Willi Syndrome Multi-Disciplinary Clinic in Sha'are Zedek Hospital in Jerusalem since 1996.He has been a member of the Professional Providers and Caregivers Board of IPWSO since 2010 and has presented in conferences in the US, Canada, England, Germany, Israel, and elsewhere.

NEIL GUMLEY, SERVICE MANAGER, MELBOURNE, AUSTRALIA. *neil.gumley@pws.asn.au*

I am the Service Manager for the only PWS specific facility in Melbourne, Victoria Australia. Our Facility houses 5 male Adults with PWS. We have been open now for 5 years. I am a board member on the Prader Willi Syndrome Association Victoria and I am the Australian Delegate for the International Professional Care Givers Board. I have managed Disability Specialised Accommodation for 15 years.

NORBERT HÖDEBECK-STUNTEBECK, PHD, DIAKONISCHE STIFTUNG WITTEKINDSHOF, GERMANY. *norbert.hoedebeck-stuntebeck@wittekindshof.de*

Dr. Norbert Hödebeck-Stuntebeck is a Psychologist, Psychotherapist and a Supervisor, who resides in Bad Oeynhausen, Germany, where he currently serves as Projectmanager Prader-Willi-Syndrome and Projektmanager Adipositas (Obesity) for Diakonische Stiftung Wittekindshof (a lutherian foundation in the north west of Germany, in Northrhein-Westfalia). He received his PhD in 2012 at the University of Eichstätt from a study about the competence of people with Prader-Willi-Syndrome (PWS) in change of emotional perspective (empathy). Since 1996 he has been responsible for the development and differentiation of support for people with PWS of all ages and in different fields of living, working, school and training programs. He is the chair of the Professional Providers and Caregivers Board (PPCB) of the International Prader-Willi-Syndrome Organisation (IPWSO) and (co)organizer of all caregiver conferences of IPWSO since the first in Romania in 2007. Since 2015 he has been the CEO of the Prader-Willi-Syndrom Institute Germany (PWS-ID). His interest in research is focused on empathy (change of perspective) in PWS and the development and evaluation of training programs. Another field is the obesity of people with mental handicaps.

PROFESSOR TONY HOLLAND, UNIVERSITY OF CAMBRIDGE, UK. *tonyipwso@gmail.com*

Tony Holland trained in Medicine at University College and University College Hospital, London, qualifying in 1973. After some years in General Medicine he trained in Psychiatry at the Maudsley Hospital and Institute of Psychiatry in London. From 1992 to 2002 he held a University Lecturer's post in the Section of Developmental Psychiatry in the University of Cambridge, and in 2002 was awarded the Health Foundation Chair in Learning (Intellectual) Disability establishing the Cambridge Intellectual and Developmental Disabilities Research Group (www.CIDDRG.org.uk). His specific research interests include the eating, behavioural and mental health problems associated with having Prader Willi Syndrome (PWS); the relationship between Down's syndrome and Alzheimer's disease, and also clinical/legal issues relevant to the needs of people with intellectual disabilities. With colleagues he has published research extensively on these topics in academic and practice-based journals. He works closely with charitable organisations and has been psychiatric advisor to, and Patron of, the UK PWS Association and since 2016 he has been President of IPWSO. In 2010 he was elected a Fellow of the UK Academy of Medical Sciences. In 2015 he was awarded a CBE in the Queen's Birthday Honours for services to psychiatry. Since October 2015 he has held an Emeritus position at the University of Cambridge.

MARGUERITE HUGHES, VICE-PRESIDENT, IPWSO. *marguerite.hughes.ie@gmail.com*

Marguerite is based in Ireland and has a 15-year-old son with PWS. Marguerite served as IPWSO Secretary from 2013-2016 and as IPWSO Vice President from 2016-2019. Marguerite has also served as Company Secretary of the Prader-Willi Syndrome Association of Ireland. Marguerite has worked in non-profit organisations in sectors including international development, homelessness, and educational advocacy for over 15 years. Marguerite holds a Doctorate in Social Science from University College Cork, Ireland.

TRINE JENSEN, BOSTEDET SOLVANG APS, DENMARK. *trine@solvangfejoe.dk*

Teacher – responsible for daily life.

DAMIEN JONES, INTERACTION, AUSTRALIA. *djones@interactionservices.org*

Damien Jones has an MBA and a Bachelor of Social Science (Social Welfare). Damien has worked as a manager for Interaction Disability Services (Interaction) for the past 14 years. Interaction established Australia's first accommodation model specifically for three adults with Prader-Willi Syndrome (PWS) in 1992 and now operates a number of PWS specific houses. Interaction also provides services such as support coordination, community participation and clinical support to people with PWS and their families.

Damien started as a Social Educator at Interaction, before being promoted to House Manager and then Senior Manager. Having worked at multiple levels, supporting people with PWS, Damien brings a unique perspective and insight into their needs. Combining his hands on perspective and management experience, Damien has delivered training and workshops on PWS to behavior intervention conferences, ADHC, internal staff members and other residential services. He has contributed to FAMCARE articles, which are available through the IPWSO website. Damien will be discussing the social aspects of ageing in people with PWS.

YOSHIRO KATO, KANSAI UNIVERSITY OF WELFARE SCIENCES, JAPAN. *gfa03452@nifty.com*

Associate Professor of Special Needs Education Course, Faculty of Education, Kansai University of Welfare Sciences. Chairman of the management committee, PWS Professional Caregivers Network operating mostly in Kansai area Japan.

NATHALIE KAYADJANIAN, PHD, FOUNDATION FOR PRADER-WILLI RESEARCH, USA. *nathalie.kayadjanian@fpwr.org*

Nathalie Kayadjanian, Ph.D is an expert in translational biomedical research in rare diseases with extensive R&D experience in academia, biotech, and the pharmaceutical industry in Europe and the USA. For the past twelve years, Nathalie has occupied top management positions in patient-driven non-profit research organizations as Associate Science Director of the French Association against myopathies (AFM) and Associate Director of biomedical research of the Amyotrophic Lateral Sclerosis Association (ALSA) in the US where she developed and implemented strategies to accelerate the development of innovative therapies for neurodegenerative and rare diseases.

Nathalie joined the Foundation for Prader-Willi Research (FPWR) in 2015 as the Director of Translational Research and has been instrumental in guiding and developing the FPWR 5-year strategic research plan. She is leading and developing a number of translational programs for Prader-Willi syndrome (PWS) including a Clinical Trial Network in the US and Canada; a Preclinical Animal Network to improve reproducibility and predictivity of PWS mouse models and serve as a drug screening platform; a biobank of induced pluripotent stem cells to support the development of PWS cell models and drug development. She is also the Executive Director of the PWS- Clinical Trial consortium that was launched in 2015 to address clinical trial challenges in PWS. She received her Ph.D in Neuroscience from the University Pierre and Marie Curie in Paris and did a postdoctoral training at the Salk Institute in La Jolla, USA.

LAURA KEANE, RESILIENCE CARE, IRELAND. *lkeane@resilience.ie*

Laura is the Managing Director of Resilience Care Ireland, a national private provider of community-based services for people with disabilities and Advanced Community Care Services caring for children with complex care needs in their own homes and communities.

Laura is a registered Occupational Therapist and has an MSc in Health Services Management from Trinity College Dublin, with over 30 years' experience working in the health and social care sector, as a clinician and then progressing into Executive Management, working across the Voluntary and Private sectors. Her passion is in delivering supports which empower andenable people with disabilities to achieve their full potential and have every possible opportunity to live a good life. She has experience in developing a culture of Continuous Quality Improvement within large scale organisations such as embracing and implementing the HIQA standards for residential services in Ireland, achieving EQUASS (European Quality Assurance System for Social Services) in day services and achieving Level 5, European Standards in Business Excellence (EFQM)

Laura is very interested in contributing to policy development at a national level and is a member of the Health Service Executive, Working Group leading the implementation of New Directions Policy and interim standards for adult day services. She was Chairperson of HSE National working group which developed the national Person Centred Planning Framework for disability services. She recently contributed to the development of national guidance in Ireland for the development and delivery of specialist services for people with PWS. She is currently a voluntary Board Member of St. Gabriel's school and centre in Limerick, which provides services for children with physical disabilities. She is the Irish Care Provider Representative to the International Prader Willi Syndrome Organisation (IPWSO).

TAKAYUKI KIDO, "IKIIKI" NON-PROFIT ORGANISATION, JAPAN. *taka.yk0209@gmail.com*

Managing Director of Non-Profit Organization ikiiki". Member of the management committee, PWS Professional Caregivers Network operating mostly in Kansai area Japan.

SVETLANA LABUN, REGENS WAGNER ABSBERG, GERMANY. *svetlana.labun@regens-wagner.de*

Ph.D., adult education, Catholic University of Eichstätt-Ingolstadt, 2004. Studies of German at the Novosibirsk State Pedagogical University, 1995. Department Manager of special services for people with Prader-Willi Syndrome at Regens Wagner Absberg since 2007. Regens Wagner Absberg is an institution for adult handicapped people offering facilities for living and working. For 20 years the institution has offered a special treatment for people with Prader-Willi Syndrome. Since this time there is cooperation with the Zentrum für Neuropsychologie – Trier and the Catholic University of Eichstätt-Ingolstadt for research on the subject of Prader-Willi Syndrome Support in the organisation of the International PPCB Conferences 2018 in Munic, 2012 in Wildbad Kreuth, 2009 and 2008 in Herne. Coach for de-escalation and management of conflicts.

CONSTANZE LÄMMER, CHILDREN'S HOSPITAL ST. BERNWARD, GERMANY. *dr.c.laemmer@bernward-khs.de*

Dr. Constanze Lämmer graduated in Medicine from the Leipzig University and received her doctoral degree in 1992 with emphasis on endocrinology. After eight years in internal medicine she started her qualification as a pediatrician and become Senior Physician at the St. Bernward Hospital Hildesheim in 2005. She is qualified in pediatric endocrinology, diabetology, nutrition,

somnology and epileptology. She established the Hildesheim program for treating patients with PWS and sees frequently more than 350 patients with PWS. In 2015 this Program was awarded the ACHSE Central prize for rare chronic disease treatment. So, she is experienced in treating patients with PWS with growth hormone but also with sexual hormones in puberty. Frequently she undertakes instructional workshops for families with PWS children in Germany and abroad. She is scientific advisor to the PWS association Germany and medical advisor for the IPWSO where she presented her work at several international conferences.

VIRGINIE LAURIER, RESEARCH ASSISTANT, HÔPITAL MARIN HENDAYE, APHP, FRENCH NATIONAL CENTRE OF PRADER-WILLI SYNDROME, HENDAYE, FRANCE. *virginie.laurier@aphp.fr*

After my master's degree in molecular Biology at the University of Toulouse, I joined Pr Hélène Dollfus' team from the Faculty of Medicine of Strasbourg for 4 years (2003 – 2006) and conducted research on Bardet-Biedl syndrome.

In 2007, I then completed a master's degree in genetic counselling at the University of Marseille. In 2008, I finally joined Dr. Thuilleaux's team as a research assistant in the French National Reference Centre of Prader-Willi Syndrome in Hendaye (South-West of France). For the last 11 years, I have worked in this multidisciplinary team that hosts (adult) patients with PWS for short stays. The purpose of the stays is to assess psychosocial and medical problems in order to define individual needs and propose a personalized management strategy. The specific objectives are weight control, improvement of physical fitness, care for medical complications, improvement of psychological well-being and social adaptation.

My main role in this team is to promote and coordinate research projects in collaboration with the other teams of the National Reference Centre coordinated by Pr Maithé Tauber in Toulouse and Pr Poitou in Paris.

GEORGINA LOUGHNAN, PRADER-WILLI SYNDROME CLINIC, ROYAL PRINCE ALFRED HOSPITAL, AUSTRALIA. *Georgina.Loughnan@health.nsw.gov.au*

Georgina has worked for Metabolism & Obesity Services, Royal Prince Alfred Hospital, Sydney, Australia since 1983. She specialises in lifestyle management of obese people with disabilities and established a public hospital-based clinic for adolescents and adults with Prader-Willi Syndrome (PWS) in 1991. She is an active member of both the local and and Australian national PWS Associations. She has been a member of the IPWSO Board of Directors for the past 7 years and regularly speaks at national and international PWS conferences. Her expertise covers physical activity, nutrition and environmental management for improved health and fitness of people with disabilities, especially those with PWS. She is a strong advocate for the spread of knowledge and understanding of PWS in order to promote good health, improved quality of life and longevity for people with PWS of all ages.

NATASA MOMCILOVIC, MAUDSLEY HOSPITAL, LONDON, UK. *Natasa.Momcilovic@slam.nhs.uk*

Natasa Momcilovic leads the PWS Assessment and Treatment Service provided by the National & Specialist CAMHS at the Maudsley Hospital in London, UK. Natasa has worked over 22 years as a Behaviour Therapist on the Learning Disabilities stream of the Service for Complex Autism & Associated Neurodevelopmental Disorders (SCAAND).Her expertise is in working with children and adolescents with complex behaviour problems and family situations. She is a trained course leader in Webster-Stratton parenting approach and has piloted a parenting programme based on the Webster-Stratton principles for parents of children with intellectual disability.

Her particular interests include parenting approaches, challenging behaviours in Prader-Willi Syndrome and feeding problems in children with intellectual disability and autism. She has developed a specialist intervention for young people with PWS which is adapted and delivered according to their personal needs and local provision.Natasa has undertaken research in treatment of challenging behaviours and published on that subject. She leads training events on management of challenging behaviours for charities, local organisations, schools and CAMHS professionals, teaches at the psychology doctorate course at King's College, London and participates in training medical trainees in psychiatry.

CRAIG MOORE, B.A. (HON) (PSYCH), DIP. REHAB. C., M. SOC. ADMIN., CEO INTERACTION DISABILITY SERVICES. *cmoore@interactionservices.org*

Craig has over forty years' experience working in the provision of welfare services to children and their families, particularly for people with disabilities. He is the CEO of Interaction, a not for profit, values based, person centered organisation, committed to empowering people with disability and their families. Interaction is a significant provider of services to people with Prader-Willi Syndrome in Australia and is expanding its services into other states.

JAMES O'BRIEN, BOARD MEMBER OF IPWSO AND CHAIRMAN OF THE PRADER-WILLI ASSOCIATION OF AUSTRALIA. *jamesob@bigpond.com*

With his powerful desire to maximize outcomes for all people living with a disability, James' management and operating experience spans national and international charities.

His expertise in Australian education and disability services have honed his lateral thinking skills with proven ability to rapidly visualize alternative processes and solutions.

Currently, James is Chairman of the Prader-Willi Association of Australia (PWSAA), Trustee of the International Prader-Willi Syndrome Organisation and a Member of the Global Genes RARE Global Advocacy Leadership Council. James is also the Founding Director and CEO of the Prader-Willi Better Living Foundation Ltd.

Fairness, compassion, and integrity, coupled with respect for the opinions, skills and beliefs of others, underscores his love for his two children and desire to establish supports for all people living with Prader-Willi syndrome, including his 25 year old son.

RAIZA PARÉS OJEDA, UNIVERSITY OF CIEGO DE AVILA, CUBA. *raizamariano@gmail.com*

I have a Bachelor's Degree in Education, majored in Special Education, with specialization in Speech Therapy. I have 20 years of experience in the educational field, and 10 years linked in the High Education. Initially I worked as speech therapist for 15 years and nowadays I am Associate Professor and the head of the Speech Therapy Career at the University of Ciego de Avila Cuba. I have a Master's degree in Educational Sciences, Specialty Special Education. I am a doctor in Pedagogical Sciences. I was hired as Professor of Special Education in Nassau, Bahamas. At present, I work as a researcher in a project dealing with Learning Disabilities in people with Prader–Willi syndrome, specifically in the language development field.

MARIA PEDERSEN, KAROLINSKA UNIVERSITY HOSPITAL, STOCKHOLM, SWEDEN. *maria.pedersen@sll.se*

Maria Pedersen, registered nurse at the endocrinology departement, Karolinska University hospital. Stockholm Sweden.

MICHAEL PETHE, DEPUTY HOME DIRECTOR, SWITZERLAND. *Michael.Pethe@argo-gr.ch*

Dipl. social pedagogue/ social worker FH, Michael is Head of Department and Deputy Home Directorworking with people with PWS since 2008. He manages two PWS residential groups in Switzerland in Graubünden. He has been a Member of the PPCB Board since 2017.

STEFAN PIMMINGSTORFER, EXECUTIVE DIRECTOR, CARITAS FÜR MENSCHEN MIT BEHINDERUNGEN/ CARITAS UPPER AUSTRIA. *Stefan.Pimmingstorfer@caritas-linz.at*

Stefan Pimmingstorfer has had the experience in the field of community based and residential housing and living support models for people with disabilities for over twelve years.

He graduated with a Master's degree in social economy from the University of Linz, Austria in 2007. He gained experience at European level as chairman of an interest group working on art. 19 of the UNBRK and he is working on an international PHD-project in Siegen, Germany.

Currently he works as an executive director and develops innovative support models for people with impaired participation in society.

HUBERT SOYER, REGENS WAGNER ABSBERG, GERMANY. *hubert.soyer@regens-wagner.de*

Ph.D., Psychology and Pedagogics, Catholic University of Eichstätt-Ingolstadt, 2003. Dissertation: Studies on social and therapeutic pedagogy of Prader-Willi Syndrome. Diploma: Psychology, Catholic University of Eichstätt-Ingolstadt, 1999. Teaching profession for Primary and Secondary School and Special Education School, 1977. Associate lecturer at the Chair for Social Education at the Catholic University of Eichstätt-Ingolstadt since 1999. General Manager of Regens Wagner Absberg since 1994. Regens Wagner Absberg is an institution for adult handicapped people offering facilities for living and working. For 20 years the institution has offered a special treatment for people with Prader-Willi Syndrome. Since this time there is cooperation with the Zentrum für Neuropsychologie – Trier and the Catholic University of Eichstätt-Ingolstadt for research on the subject of Prader-Willi Syndrome. IPWSO Board: Co-opted Board member, June 2011. Professional Providers & Caregivers' Advisory Board: Board member. Organizer of the International PPCB Conferences 2018 in Munic, 2012 in Wildbad Kreuth, 2009 and 2008 in Herne, Germany together with Dr. Norbert Hödebeck-Stuntebeck and the Board members of PPCB. Managing director in the newly established non-profit company Prader-Willi-Syndrom Institut Deutschland gGmbH (PWS-ID).

JORGELINA STEGMANN, MD, SPINE FOUNDATION, ARGENTINA. *jstegmann@spine.org.ar*

Jorgelina Stegmann is a clinician graduated from the Faculty of Medicine of Buenos Aires University (2002), with specialization in Psychoinmuno_neuroendocrinology from Favaloro University (2004) and magister in Psyconeuropharmacology. She also studied Management and Direction of Institutions in Health (Austral University, 2015) and currently doing the Executive Master Business Administration at IAE University. Since 2004, Jorgelina has been president of Fundación SPINE, member of the Latinamerican PWS Committee, and member of the Rare Diseases Committee at the National Ministry of Health and Social Development. Before that, she worked in internal medicine services at public hospitals and private clinics.SPINE Foundation is a non-for-profit organization founded in 2005 in Buenos Aires, Argentina. Its purpose is to provide for clinical diagnosis, assistance and treatment to people affected by rare disorders. Its therapeutic approach is based on the system called social. psycho.immune.neuro.endocrinological (S.P.I.N.E.), which allows for a comprehensive outlook of patients and their environment, in accordance with each disorder. Formed by a team of health professionals, including general physicians, psychiatrists, psychologists, physiatrists, physical therapists, nutritionists, occupational therapists, PE teachers and therapeutic assistants, SPINE Foundation works in a transdisciplinary way with the commitment of promoting full development and a better life quality for patients and their families.

YASUNOBU YAMADA, RESIDENTIAL REHABILITATION INSTITUTION "TERAN HIROBA", SOCIAL SERVICE ORGANISATION "DOYUKAI", JAPAN. *yasunobu@fa3.so-net.ne.jp*

Chief Assistant of Residential Rehabilitation Ins-titution "Teran Hiroba", Social Service Organization "Doyukai". Head of the management committee, Kanto area Japan PWS Professional Caregivers Network Director of PWSA Japan.

PROFESSIONAL PROVIDERS' AND CAREGIVERS': SPEAKER ABSTRACTS

SESSION 1: OPENING AND OVERVIEW ABOUT SPECIAL PROVISIONS AND SERVICES FOR PWS IN DIFFERENT COUNTRIES

OVERVIEW CUBA: ATTENTION TO PEOPLE WITH PRADER-WILLI SYNDROME FROM THE PERSPECTIVE OF SOCIAL INCLUSION

▸ **Raiza Parés Ojeda, University of Ciego de Avila, Cuba**

Prader–Willi syndrome is a complex genetic disorder affecting multiple body systems. Attention to the people with Prader-Willi syndrome has as a foundation the focus of integral attention to the people with special educational needs, where the process of characterization and diagnosis has paramount importance. This attention must not be conceived from a perspective purely curricular, centered in direct work with the pupil, but very singularly like a system of stock structured that implicates the family and the rest of the community agents and agencies. Cuba has the conditions required to offer the persons with Prader-Willi syndrome the proper attention through the utilization of a coherently articulated system what it makes possible an adequate incorporation to the work and social life as a hard worker in the society with equal rights. The objective of this presentation is explaining the conception of the attention to the people with Prader-Willi in Cuba from the perspective of social inclusion.

OVERVIEW AUSTRALIA

▸ **Craig Moore, B.A. (Hon) (Psych), Dip. Rehab. C., M. Soc. Admin., CEO Interaction Disability Services and Neil Gumley, Service Manager in Melbourne, Victoria Australia. Board member of the Prader Willi Syndrome Association Victoria and Australian Delegate for the International Professional Care Givers Board.**

People with Prader-Willi Syndrome (PWS) have been disadvantaged and disenfranchised within the Australian disability sector due to a lack of understanding of their unique needs, particularly in the provision of worthy accommodation. Accommodation for people with PWS has suffered in Australia from a misplaced philosophical position by governments and providers of placing people with PWS, who require high support accommodation, into generic group homes. Only a few specific PWS specific accommodation programs have been developed in Australia over the past 25 years and these have been given euphemistic names such as The Specialist Community Program and The Healthy Eating House. Placing people with PWS into generic programs has caused great distress to the individuals with PWS, their families and the organisations attempting to cater for the divergent needs within these programs. Australia has introduced The National Disability Scheme (NDIS) to provide for all people with disabilities. Its stated philosophy is to provide individuals with the reasonable and necessary resources for that person to live an ordinary life. It is intended to allow individuals and families to choose the type of accommodation best suited to the individual's needs. Jurisdictions in Europe and North America, where there is a clearer understanding of the unique needs of people with PWS, have funding models which have been developed to specifically support people with PWS. This presentation will discuss what services are currently being provided in Australia and the different models of accommodation and service delivery being developed for the Australian context and funding models under the NDIS.

OVERVIEW ARGENTINA

▸ Jorgelina Stegmann, SPINE Foundation, Argentina

SPINE (Social-psicho-immuno-neuro-endocrinology) foundation is an institution that works upon the approach of rare diseases (RD) and especially focused in Prader Willi syndrome (PWS) since 2004. Its transdisciplinary approach aimed at the evaluation, research and treatment, offers an integral and comprehensive appraisal of both patient and family; encompassing diverse fields such as medical (internal medicine), psychiatry, psychology, psychopedagogy, phonoaudiology, psychiatry, occupational therapy, and nutrition. The role of the caregivers is complementary to the team of professionals, carrying out various physical, recreational and cognitive stimulation activities supervised by our treatment team.

While the patients' transdisciplinary approach is being carried out, their parents work with other professionals upon the reeducation of the syndrome.

In brief, the main objectives of the transdisciplinary approach involve the assessment and treatment of behavioral problems, nutritional management, reeducation of the syndrome and physical rehabilitation, among others. There is a tailored plan for each patient, established by the treating team that sets therapeutic objectives that are henceforth enhanced by the caregivers. Patient surveillance is performed through weekly, mid-term and annual reports that are discussed in weekly clinical athenaeums involving professionals, coordinators, and caregivers, where the therapeutic objectives are defined, and the evolution of the patient is reported. Both patients' and their respective families are treated on a weekly basis from these aforementioned perspectives.

Some of the main results of that we have achieved can be summarized as follows. At admission, 42% of patients presented morbid obesity, 38% grade II-II obesity, 4% overweight, 12% normal weight, and 4% a low weight. Currently, we have attained significant improvements in this regard, with rates of morbid obesity of 11%, grade I-II obesity of 35%, overweight in 35% of patients, normal weight in 19%, and no patients with low weight. In relation to psychiatric medications on admission, 42% arrived, currently there are 58% and 7.69% was suspended. During the admission process, the medication plan was modified, in some cases suspended. Currently, all patients are stable from a psychiatric and clinical perspective, under weekly supervision. Furthermore, a number of diverse other clinical conditions were identified, including sleep disorders and cardiac manifestations among others; and specific treatment for these have been established accordingly.

OVERVIEW IRELAND

▸ Laura Keane, Resilience Care, Ireland

Laura's presentation will give an overview of the services for people with Prader Willi Syndrome in Ireland, in particular the recent progress being made in developing new national guidelines and specialist supports for people with PWS.

OVERVIEW JAPAN: ADULTS WITH PWS AND CAREGIVERS' NETWORKS IN JAPAN

▸ Yoshiro Kato, Kansai University of Welfare Sciences, Japan. Takayuki Kido, "ikiiki" non-profit organisation, Japan. Yasunobu Yamada, Residential Rehabilitation Institution "Teran Hiroba", Social Service Organisation "Doyukai", Japan

In Japan, most adults with PWS live with their parents almost permanently.

Their daily lives depend heavily on their family. And there are also no group homes specialized for person with PWS. The reason for such situation is that it is not enough for welfare participants and so on to understand their behavioral characteristics and developmental traits of people with PWS, and there are still no special services for PWS, such as 24 hours around-the-clock care or supervise services. In addition, employment rate of them is seriously lower than that of people with other intellectual disabilities maybe caused by their probabilities of behavior problemsμKato et al., 2015).

In these conditions, we each established PWS caregivers' network at Kansai district in 2004 and Kanto district in 2011.

And we have convened case meetings and study sessions several times every year. Besides former network published their activity and case report collections at their own expense in 2011 and this year. So we'll mainly introduce some information on adults with PWS in Japan and our networks' activities, and suggestions found from case reports of Kansai Network. For example, some procedures of positive behavioral supports (PBS) are effective.

SESSION 2: EARLY INTERVENTION

MAIN CHALLENGES IN ADULTS WITH PWS

▸ Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof , Germany

To start a presentation about early intervention with challenges in adult people with PWS seems to be surprising. But the idea behind this is, that in a first step we have to know which problems/ challenges we see in the adults with PWS and in the second step to know how the development of these challenges is. If we understand the way these problems started and develop over the life span, we have the change to influence them in a positive way and reduce the frequency and intensity of them.

Hyperphagia and complications of obesity, skin picking and intellectual disabilities, the behavioral phenotype, social challenges and mental health concerns are the main challenges we will discuss in this presentation.

PHYSICAL DEVELOPMENT AND CHANGES IN CHILDREN WITH PRADER-WILLI SYNDROME: THE FIRST SIX YEARS OF LIFE

▸ Constanze Lämmer, Children's Hospital St. Bernward, Germany

Introduction: Prader-Willi Syndrome is a complex neurogenetic disorder. The holistic treatment approach includes the major nutritional management, movement therapy and growth hormone treatment. It is postulated, that behavioral problems later in life have their origin early in childhood. Moreover, a psycho-pedagogical guidance for the families should be included in the treatment concept.

Methods: The presentation shows the physical development in the domains motor function, speech, senses in the first six years and the delays in children with Prader-Willi-Syndrome.

Summary: Children with Prader-Willi-Syndrome reach milestones in all developmental domains later in life than their peers. The delay is caused by muscular hypotonia and disturbed brain development. Interactive playing with other children of the same age is difficult. Children with Prader-Willi-Syndrome need an early intervention. Their parents need professional support. Therefore, there is a need to develop a Prader-Willi-Syndrom specific early intervention program.

COGNITIVE, EMOTIONAL, SOCIAL DEVELOPMENT

▸ Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof, Germany

The life span from 0 to 6 years is the part of life, where we develop the basis for so many competences which we need when we have to handle the tasks in the adolescent period and in the adult time of life. In this presentation will be described the normal development in the periods from 0 to 6 months, 6 months to 1.5 years, 1.5 year to 3 years and from 3 to 6 years. In each period we describe the normal development of the cognitive,

the social and the emotional competences. It will be discussed what is different in PWS and which kind of support is possible to support the competences in this field.

PARENTS AND ENVIRONMENT

▸ Constanze Lämmer, Children's Hospital St. Bernward, Germany

Prader-Willi Syndrome is a complex neurogenetic disorder. Beside the management of the uncontrolled appetite the management of the obsessive compulsive and demanding behavior is a special challenge for the families and caregivers. Children with Prader-Willi syndrome reach the milestones in cognitive, emotional and social development later and incompletely. Parents and environment can support children in their development from early beginning on. Infants with PWS give less signals, so parents have to look for small changes. Age adapted offers are needed to satisfy basic needs. Children have to learn to express and become aware of emotions. Later they need help to overcome egocentrism and to be able to facilitate social interactions. Breaking routines can help to become more flexible. Children with PWS need always support to manage such tasks. Children with PWS need positive role models and a feed back to learn acceptable behavior. Therefore, there is a need to develop a Prader-Willi-Syndrom specific early intervention program. First ideas, how parents and environment can support children with PWS to complete these developmental tasks will be given.

SESSION 3: PWS AND AGING

MEDICAL AND COGNITIVE ASPECTS OF AGING

▸ Larry Genstil, PhD, Member of PPCB, Psychologist of the PWS Multi-Disciplinary Clinic at Sha'are Zedek Medical Center, Jerusalem, Israel, Owner and Professional Director, Genstil Hostel for People with PWS

▸ Damien Jones, Interaction, Australia

Since people with PWS have extended life spans during the past couple decades, there are several areas in which aspects of aging have become apparent: Medically, there are many signs of early onset of various health issues which will be presented.

Cognitively, again there are many signs of early onset of various issues affecting quality of life, functioning, etc. Socially, again there are issues which will be presented by Damien Jones.

Since in the past, most people with PWS never reached advanced age, these declines were not known. We are at a preliminary stage of discovering all the various areas of early signs of aging in this population. This is a serious issue as now there are many people with PWS living into their 50s, 60s, and even beyond. Their need for services will only expand as they age.

EMOTIONAL ASPECTS OF AGING

▸ Larry Genstil, PhD, Member of PPCB, Psychologist of the PWS Multi-Disciplinary Clinic at Sha'are Zedek Medical Center, Jerusalem, Israel, Owner and Professional Director, Genstil Hostel for People with PWS

▸ Damien Jones, Interaction, Australia and Member of the PPC and Famcare boards of IPWSO

SOCIAL ASPECTS OF AGING: ACTIVE AGING WITH PWS

▸ Damien Jones, Interaction, Australia and Member of the PPC and Famcare boards of IPWSO

Improvements to health care have combined with a better understanding of how to live a healthy life with PWS. As a result of this, many people with PWS are living longer lives. This presentation will discuss some practical challenges that need to be considered by those that support people with PWS as they age.

Damien Jones has been managing shared accommodation for people with PWS for over 14 years and currently supports a number of people with PWS in their 50s. We have found that it is possible to continue an active routine as people with PWS age. In fact, some people are still able to go on 10km hikes or swim 40 laps of a pool. However, we have also experienced the progression of chronic health conditions, such as diabetes, sleep apnea and mobility issues related to poor bone density which can impact social inclusion. Support Workers report increased confusion in those aging with PWS. We have found that some people with PWS struggle to continue to work full time. There are concerns for the future, when ageing parents are no longer able to care for those with PWS in the same ways that they did in the past. Finally, there is a lack of knowledge regarding PWS in aged care systems. This presentation will discuss these issues and the impact aging has on the social life of people with PWS.

SESSION 4: HANDLING CRISIS SITUATIONS AND CHALLENGING BEHAVIOUR

SYSTEMIC VIEW

▸ Norbert Hödebeck-Stuntebeck , Diakonische Stiftung Wittekindshof, Germany

Challenging behavior and crisis situations are well known phenomena in taking care of people with PWS. Therefore, there is a big need to be able to handle situation like this. In the following presentations about prevention, handling and reflection will be described detailed information, ways and methods to be more competent in these three steps.

At the beginning there will be described the systematic view about challenging behavior and crisis, to show how complex these situations are and how many stakeholders are involved in these situations and influence these situations and the results. Also there will be an introduction to the way a challenging behavior starts.

LEGAL BASICS AND ETHICS: RESTRICTIVE PRACTICE IN THE CARE OF PEOPLE WITH PRADER-WILLI SYNDROME – A REVIEW OF THE LITERATURE

▸ Anna Murray, University of Cambridge, UK (presented by Professor Tony Holland)

There is a dilemma in the care of people with Prader-Willi Syndrome (PWS) – how do we balance the rights of people with PWS and provision of good care? Is it ethical to restrict their behaviour in order to prevent the damage caused by overeating? By placing early restrictions on people with PWS do we in fact foster liberty in the future?

Parents, carers and authorities struggle with the tension between maximising individual choice and control, satisfying carers duty of care and providing a safe workplace for support workers. There is a need for clear, justifiable, evidence-based guidelines for the care of adults with PWS, which are consistent with international human rights law and are possible to implement in a variety of settings around the world. The 'Choice and Control' project aims to produce such guidelines.

As part of this project, we have undertaken a review of law regarding restrictive practices for people with PWS in multiple jurisdictions. Key themes that have emerged include the need to define 'restriction' according to the patients' expectations and the importance of resource allocation. We will present our findings and discuss how they relate to the development of guidelines on restriction of access to food and which service providers are best suited to do this.

PREVENTION

- Svetlana Labun, Regens Wagner Absberg, Germany
- Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof, Germany

The best challenging behaviors are the challenging behaviors which did not happen. If this sentence is correct, then one main focus in our all day care of people with PWS must lay on the prevention of challenging behavior.

In the education and assistance of people with Prader-Willi syndrome, there are always situations and behaviors that challenge parents and caregivers in a special way. They can express themselves in verbal confrontations or in physical aggression or maladaptive behaviors. This lecture focuses on the handling and understanding of these situations and behaviors. These methods and options were developed from the experience of many caregivers and collected during conferences and workshops in IPWSO over the last years.

On the basis of systemic understanding, various components are considered that play a role in the emergence of behavior. The structures and framework conditions in which the person lives with PWS and in which parents and employees act (environmental factors) are considered. In the same way, we consider the person with PWS with syndrome-related but also individual characteristics. In addition, possible shares of the actors in the development and course of behavior are described and included in the process of understanding. Ultimately, identifying and considering the interaction between all these components is a major challenge in the process of understanding and coping with crisis situations.

HANDLING

- Michael Pethe, PPC Board and Deputy Home Director, Switzerland

In the presentation I will show the way from a crisis to a temper tantrum by a model of seven phases. The model will be explained step by step and you will get concrete tips in handling and understanding the circle of a crisis. The focus of the presentation is in how to deal with the behaviour of the people with Prader-Willi Syndrome in the different phases and what can be done to cool the situation down. Especially I will show what kinds of possibilities you have during the escalation phase.

REFLECTION: Concrete support within a Rogerian practice framework

- Christine Ford, Community Connections, New Zealand

Reflection: Concrete supports used to have difficult conversations with people with Prader-Willi syndrome within a Rogerian practice framework: The use of objects and visual strategies to assist people with Prader Willi Syndrome to externalize triggering topics.

Positive behaviour support remains a cornerstone of managing behaviours typically associated with Prader-Willi Syndrome. Confronting the person with Prader-Willi Syndrome about concerning behaviour can trigger the behaviours under discussion. This presentation argues that positive outcomes can be achieved by adopting Rogerian practices while debriefing people with Prader-Willi Syndrome and then working with them to identify possible replacement behaviours.

Features of this kaupapa (Maori = framework) include focussing the discussion towards neutral stimuli and concepts without risking the perception of threat for the person. By objectifying and externalising the behaviour the person can contribute ideas freely towards problem solving and reflection, and then work out how to apply it to their own personal context. The behaviour specialist maintains unconditional positive regard for the person and uses objects/drawings and visuals to externalise the subject matter. These discussions can be used to inform debriefing, planning discussions, responsibility taking and identifying replacement behaviours.

FRIDAY 15TH NOVEMBER

SESSION 5: PEOPLE WITH PWS AT HOME - FAMILY SUPPORT

BASICS FOR FAMILIES: WHAT DO FAMILIES NEED? A TIRED PARENT'S PERSPECTIVE ON CARING FOR A TEENAGER WITH PWS AT HOME

- Marguerite Hughes, Vice-President, IPWSO

Most people with PWS are raised by their families and many continue to live in their family homes throughout their lives. Services, supports and information for families deserve, therefore, to be a key consideration for all professionals with an interest in PWS. Families may reasonably wonder about the appropriateness and quality of the services, support and information they receive.

So, what do families caring for people with PWS at home need? And who decides this? How can the quality of services, supports and information be assessed? Is it possible to have too many services, too much support, and too much information?

Based on personal experience of caring for her 15-year-old son, as well as research conducted with families of people with PWS in Ireland, the presentation will discuss these and other questions.

MODEL OF A SPECIALIST MENTAL HEALTH / BEHAVIOURAL SERVICE FOR YOUNG PEOPLE WITH PWS

- Natasa Momcilovic, Maudsley Hospital, London, UK

Despite PWS being associated with intellectual disability and often significant behavioural disorder in childhood and adolescence access to CAMHS can be difficult when there is no clear evidence of mental health disorder. Emergence of psychiatric illness in later adolescence mostly associated with maternal disomy type of inheritance activates referral to CAMHS, yet it is the younger children with PWS, their families and care givers who can mostly benefit from an early intervention.

National and Specialist CAMHS Learning Disabilities team at the Maudsley Hospital in London offers a unique service that bridges this gap by providing full psychiatric assessment and treatments recommended by the National Institute for Health and Clinical Excellence (NICE) including behavioural/cognitive therapy, medication combined with psychological therapies, advice on management of behavioural problems at home and at school, liaison with local services and support around transition to adult services.

PWS clinic has been operating for the past 5 years and recent service evaluation demonstrates significant increase of parental understanding of the impact of PWS on behaviour of young people, improved parental behaviour management skills and increase in scores from referral to discharge as measured by Children's Global Assessment Scale. Overview of the work of PWS clinic will be presented, including clinical examples of joint working with local services, and recommendations for dissemination of knowledge and experience discussed.

NUTRITION IN A FAMILY ENVIRONMENT

- Constanze Lämmer, Children's Hospital St. Bernward, Germany

Prader-Willi Syndrome is a complex neurogenetic disorder. After birth infants with PWS show muscle hypotonia and feeding difficulties. It is important to feed enough to receive the necessary nutrition required for adequate growth. Later children with PWS are more interested in food. The period after starting complementary food is important for characterize taste. Children learn rules at the family table and this makes meals and daily life easier for the family. The children get a well-balanced diet rich of vegetable and fruits. The energy intake is adapted to the energy expenditure. Usually it is around 60-70 % of the peers. More energy can be given, if the children with PWS are very active and build up muscles. At the beginning meals and

environment are controlled by the parents. They give the child security and structure. Depending on age, development of the child and the situation of the family, children with PWS can learn to become partially responsible for their nutrition in a well-defined setup. Frequent weight control proves the child is mature for this. Often, teenager show fewer behavioral problems if they get a chance to take decisions on their own.

PHYSICAL EXERCISE IN A FAMILY ENVIRONMENT

▸ Georgina Loughnan, Prader-Willi Syndrome Clinic, Royal Prince Alfred Hospital, Australia

Prader-Willi syndrome (PWS) is known as the most common genetic cause of life-threatening obesity. Good care and lifestyle management of people with PWS is as essential as is limiting their energy intake to avoid obesity. However, physical activity is important for more than just weight management. People with PWS have specific musculo-skeletal deficiencies that can be improved through exercise. Growth hormone therapy, when it is available to children with PWS, can be of great benefit to health and development, but only when a healthy lifestyle, that includes regular and effective exercise, is practised. Obesity related health problems, such as oedema, diabetes, hypertension, as well as mood and behaviour can all be improved with exercise. This presentation discusses the essentials of exercise for people with PWS, especially within the family environment.

SESSION 6: TEACHERS' WORLD

ISSUES WITH TEACHING PEOPLE WITH PWS IN THE CLASSROOM: THE CHILD WITH PWS IN THE CLASSROOM

▸ Larry Genstil, Genstil Institute of Human Behaviour, Israel

When teaching a classroom in which a child with PWS is included, there are several issues that need to be addressed in order to maximize the learning of the PWS child:

1. Food security
2. Behavior management
3. Visual vs. auditory perception
4. Social involvement
5. Teaching social skills
6. Teaching empathy
7. Parental involvement

The above issues will be discussed with recommendations to enhance the classroom environment for the PWS child and all the other children in the classroom.

SESSION 7: NEUROPSYCHOLOGY IN PWS

A NEUROPSYCHOLOGICAL VIEW OF PWS

▸ Hubert Soyer, Regens Wagner Absberg, Germany

▸ Svetlana Labun, Regens Wagner Absberg, Germany

Neuropsychology is an interdisciplinary branch of brain research and seeks to understand the relationship that exists between behavior and the brain, that is, it intends to explain how brain activity manifests itself in observable behavior.

Neuropsychology deals with questions such as:

What mechanisms are responsible for thought, learning and emotion in people with PWS?

How do these mechanisms work?

The core features of the syndrome are hypotonia, hyperphagia, growth deficiency, and hypogonadism. Cognitive impairment, emotional dysregulation, behavior problems, communication problems and impaired social skills have a particularly strong effect on everyday life. Abnormalities of brain structure and function have been described through neuroscience literature, but we are just beginning to understand the development of the brain in PWS, the dynamics of its interconnections, and the impact of interventions such as hormonal supplementation, psychotropic medication or various kinds of therapies.

Main focus of the talk are the functional deficiencies of the Hypothalamic-Pituitary axis in people with Prader Willi Syndrome and their effect on observable behavior.

The talk will pay special attention to possible interventions and coping mechanisms that allow people with PWS to improve their quality of life.

SESSION 8: SCIENCE AND RESEARCH

OVERVIEW OF PWS RESEARCH THEMES

▸ Tony Holland, University of Cambridge, UK

Prader-Willi Syndrome (PWS) is a complex genetically determined syndrome in which many organ systems of the body are affected resulting in a recognised atypical pattern of development and with specific physical characteristics and a high risk of particular behavioural problems, the emergence of hyperphagia in early childhood, and an increased risks of mental and physical ill-health. These can all impact on wellbeing and the quality of life of the person with PWS and of their families and other caregivers. Research seeks to use systematic approaches to understand the links between genotype and the physical and behavioural phenotype and through this understanding to develop and test interventions and treatments that may bring benefit. With different insights resulting from the application of basic and applied research, a more coherent understanding of PWS has developed. Early diagnosis, which is now possible through a knowledge of the genetics of PWS; a better understanding of many aspects of PWS; the use of growth and sex hormone supplementation; and more effective and informed ways of supporting people with PWS have all followed from diverse strands of research. I will review where we are now and the potential for new understanding and treatments.

CURRENT AND PLANNED FUTURE CLINICAL TRIALS

▸ Nathalie Kayadjanian, Foundation for Prader-Willi Research, USA

Clinical trials have been fundamental in fostering the development of novel treatments in medicine and for understanding disease mechanisms. Since 2012, the number of clinical trials testing new drugs for PWS has been multiplied by four. Drugs with different mechanisms of action are being tested opening avenues for better understanding the biology underlying PWS. While this raises the hope that new treatments will be available in the near future, there are a number of challenges and barriers at each stage of the therapeutic development process that could impede successful clinical trials outcomes and access to meaningful therapies for individuals with PWS. An overview of clinical trials in PWS and efforts undertaken by the PWS community to address challenges will be discussed in the context of the specificities of rare diseases and PWS.

ICEBERG ALERT: SYSTEMATIC SCREENING REVEALS LARGE NUMBER OF UNDETECTED HEALTH PROBLEMS IN ADULTS WITH PRADER-WILLI SYNDROME

▸ Laura de Graaff, Erasmus MC Rotterdam and Dutch Center of Reference for Prader-Willi Syndrome

Introduction: In Prader-Willi Syndrome (PWS), up to 3% of patients die every year. In half of the patients, the cause of death is of cardiovascular origin and / or obesity-related. Cardiovascular problems have a multifactorial origin, most of which relate to an excess of energy intake, compared to energy expenditure. On the one hand, excess energy intake due to overeating can cause morbid obesity, leading to diabetes and secondary cardiovascular complications. On the other hand, energy expenditure is low due to low muscle mass, which can further deteriorate due to undetected hormone deficiencies (like hypogonadism, hypothyroidism and GH deficiency). On top of this, fatigue (due to undetected hormone and vitamin deficiencies) can reduce exercise tolerance, thereby further increasing obesity. Due to the behavioral phenotype of PWS (patients do not report pain and hardly ever complain about physical problems), hormone deficiencies and other comorbidities often remain unnoticed. Undetected co-morbidity can lead to medical complications, requiring admission to the hospital ward or intensive care unit. Systematic screening can prevent part of the personal and financial burden of undetected comorbidity. In order to reveal yet undetected health problems, we performed a systematic health screening among adults with PWS.

Methods: We systematically screened 106 adults with PWS (mean age 31.3 ± 12.0 y) for the presence of (undetected) health problems. Based on a medical questionnaire, medical file search, extensive interview, thorough physical examination and biochemical measurements we made an overview of the health problems already diagnosed and those detected by our systematic screening.

Results: We found a striking number of undetected and untreated health problems and health risks. Undetected health problems (like hypogonadism, diabetes, hypothyroidism and hypertension) were present in 69% of the patients. 37% even had multiple undetected health problems at the same time. The most common health problems were hypogonadism (100% in males and 78% in females), vitamin D deficiency (51%) and scoliosis (44%). We also found many untreated health risks: 30% of the patients was not on a diet and 20% exercised less than 30 minutes a day.

Conclusion: We detected a striking number of untreated health problems and health risks among adults with PWS which, if left untreated, can pose a serious health threat. Systematic screening is needed to detect these problems in an early phase. This will prevent complications and might even reduce mortality in this vulnerable patient population.

IMPROVING CARE OF PRADER-WILLI SYNDROME: EVALUATION OF A NEW CARE PROGRAM COMBINING ADAPTED PHYSICAL ACTIVITY, NUTRITION AND THERAPEUTIC EDUCATION

▸ Virginie Laurier, Hôpital Marin Hendaye - AP-HP, Unité Prader–Willi, Hendaye, France

Introduction: Prader-Willi syndrome (PWS) is a rare and complex genetic disease characterized by hypothalamic-pituitary axis dysfunction combining eating disorders associated with hyperphagia and satiety deficiency, mild intellectual deficit and behavioral disorders. This disease requires continuous management through specific therapeutic education to prevent metabolic and cardiorespiratory complications related to obesity. Physical activity must therefore be regular, adapted to the disability, taking into account cognitive deficits and behavioral disorders. The presented study aimed to evaluate an innovative and individualized care program combining Physical activity, Nutrition and therapeutic education for adults with PWS who have been admitted to our hospital for 1 month.

Methods: Twenty-one adults PWS patients,16 females and 8 males (median age: 30.4 years [min 20.8-max 58.1]; median BMI 47.3 kg/m² [min 26.6-max 68.3]) admitted to our hospital were enrolled in this study. The program includes: 2 days of assessments allowing the medicine to prescribe a physical activity program adapted to the patient's phenotypic profile, based on indoor or pool sports or physiotherapy sessions. For 4 weeks, patients, in addition to their physical activity program, will benefit from group workshops on nutrition and physical activity, and meal simulations to assess eating behavior. After the 4-week program, patients are reassessed to measure their physical and functional abilities and metabolic parameters. The benefits of the program on eating behavior, observance of the program and on the weight curve is also measured.

Results: The results showed, after the program, an improvement in physical abilities (6-minute walk test: +9.5%) and respiratory parameters (+ 8%), an interesting weight loss (-3.7% of BMI) and a good observance of the physical activity program (90.5% of the patients). However, the eating behavior does not show any significant improvement with the evaluation grid used. It seems that this would require more group workshop sessions.

Conclusion: This study demonstrated that an innovative and individualized care program combining Physical activity, Nutrition and therapeutic education for adults with PWS can lead to significant improvement in various clinical and behavioral parameters. However, these preliminary results should be confirmed by a double-blind randomized study with a larger number of participants.

PROJECT ECHO: TRANSFERRING KNOWLEDGE THROUGH CASE-BASED LEARNING AND TELEMENTORING

▸ James O'Brien, Board member of IPWSO, Australia

In partnership with the ECHO Institute, University of New Mexico, IPWSO is establishing a working group to consider how the model put forward by the ECHO Institute can be used to develop and maintain 'communities of good practice' in the diagnosis, treatment and support of people with PWS around the world. The aim of project ECHO is stated as 'democratising knowledge' through the use of internet-based technology to support skills development in countries where such skills do not exist in order to leverage scare resources, develop best practice, use case based learning to help local individuals manage complex situations, and to monitor outcomes. The support of people with PWS critically depends on the skills of family members and paid support staff together with having access to expertise to address health needs - this is a challenge in many parts of world particular given that PWS is a rare disorder. Project ECHO may prove one way of doing this complementing IPWSO's work providing individual support, participating in workshops and organising conferences.

SESSION 9: NEW DEVELOPMENTS

STANDARDS - HOW TO DEVELOP FIRST IDEAS

▸ Laura Keane, Resilience Care, Ireland

This presentation is made by me not as an expert but as someone interested in raising the ideas and rationale for the strategic development of standards. I have made contact with people who are involved in developing standards and my presentation has been influenced by their comments. I will use the presentation as an introduction to developing an international quality assurance system for PWS.

DEVELOPING SUMMER CAMPS FOR PEOPLE WITH PWS

▸ Michael Pethe, PPC Board and Deputy Home Director, Switzerland

I will give a short overview of how this project arose from the group of Caregiver Delegates. Who are the organizers? Where will it happen? Who can participate? What will be in the program?

Developments in PWS in Austria

Stefan Pimmingstorfer, Executive Director, Caritas für Menschen mit Behinderungen/ Caritas Upper Austria

After a brief overview of the current situation in Austria, developments in one of Austria's nine federal states - in Upper Austria - are in the foreground. The presentation gives an overview of the results of scientific cooperation with the University of Applied Sciences in Upper Austria. These are support models and accompanying offers developed for people with PWS who want to live or already live in St. Pius, Caritas. In Austria there is no official home for people with PWS, so many Austrians with PWS live in Germany. Caritas in Upper Austria started to develop an official offer a few years ago with the support of Germany (PWS-ID) and the PWS Austrian association. The presentation outlines the success so far and some challenges.

Supporting health situations in Fejo, Denmark: "An Island in the sun"

Karin Birkedal, Bostedet Solvang ApS, Denmark

Trine Jensen, Bostedet Solvang ApS, Denmark

Christina Brydegaard, Bostedet Solvang ApS, Denmark

An introduction to how we on a small Island in Denmark have organised living – and having a meaningful "job" for our residence with PWS. We will show/tell how health care is included and how we practice "hidden motion and movement". In our video, we will show what a day can look like, the apartments, the different workplaces, free time activities and food situations.

TRANSITION – THE ROLE OF THE ENDOCRINE NURSE

▸ Maria Pedersen, Karolinska University Hospital, Sweden

Introduction: In the transition phase of young adults with PWS it is important to get knowledge of current medical treatments problems and needs, learning about the patient's strengths and challenges, explaining and implementing new routines. In clinics without multidisciplinary transition the adult endocrine nurse has an important role during the transition phase. To standardise the process, we have developed a check list for the nurse transition.

Methods: Description of development transition between the paediatric nurse and the adult endocrine nurse in a clinic without multidisciplinary transition teams.

Results: At the transition time the young adult with parents and the paediatric and adult endocrine nurses meet in the paediatric clinic. Individual problems and needs are discussed and in case of treatments needing assistance with administration, like GH and Testosterone, plan for further nurse visits. New routines at the adult clinic are introduced like assessment of body composition with bioimpedance.

When the patients came to visit the adult clinic after the introduction of the new transition check list, they were calmer and more confident. Collection of information on current needs and problems and performance of measurements was more easy and clear. The introduction of bio-impedance was well-accepted, and none refused. The family members also explained their satisfaction with the nurses' involvement in the plan for future care.

Conclusions: Nurse meetings helps increasing the confidence of the patient with PWS in transition. For any adolescent, the transition from paediatric to adult care is a challenge aiming at more independent care and working with new adult providers. Transition of patients with PWS from paediatric to adult care needs special and careful considerations.

PROFESSIONAL PROVIDERS' AND CAREGIVERS' CONFERENCE: POSTER ABSTRACTS

#1 NORO, A RESOURCE CENTRE FOR PWS AND RARE DISEASES

▸ Authors: Dorica Dan, president RPWA, Dan Tiberiu, parent delegate IPWSO, CEO RPWA;
Romania, Romanian Prader Willi Association, NoRo Center, Zalau, str. 22 Decembrie 1989, nr.9, jud. Salaj;
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Introduction: Romanian Prader Willi Association through NoRo Center is providing integrated care to improve the quality of life for patients with Prader Willi Syndrome and other rare diseases and bridging the services and the professionals in order to ensure continuity of care at local, national and international level.

Methods: improve care services for patients with PWS to ensure continuity of care through integrated care services, case management and establishment of inter-sectorial and public-private partnerships for monitoring and assessment of the rare diseases patients needs and create networks in community to address their needs;

NoRo Center has been opened in 2011 through a Norwegian grant and a mentoring program with Frambu Resource Center for Rare Diseases in Norway and since then, we have continued to improve our services to ensure continuity of care through integrated care services and case management under INNOVCare project - Innovative Patient-Centred Approach for Social Care Provision to Complex Conditions. In 2016 we established Ro-NMCA- ID (Network Multiple Congenital Abnormalities with Intellectual Disability) and became memers of ERN ITHACA, in 2017 we were accredited by Ministry of Health as a Center of Expertise for rare diseases and autistic spectrum disorders.

Initiated the European network of resource centres for rare diseases RareResourceNet. NoRo Center, Frambu and Agrenska were the steering committee of this network.

Results: 140 – 150 patients and personal assistants/ year in groups, 60 children in Day Care Center, more than 400 requests solved on HelpLine, 3-4 workshops and trainings organized/ year and around 200 people / year attending conferences; We organize a group of 12-14 patients with Prader Willi Syndrome and other rare diseases every month, together with their personal assistant for a week, from Monday to Friday, facilitating activities of support group, psychological counseling, evaluation of an interdisciplinary team and therapeutic education for parents and access to therapies for children and young people with PWS from all over the country. During the week at NoRo, we offer patients: interdisciplinary assessment, behavior therapy, nutrition management, speech therapy, gymnastic, hydro, ergo and occupational therapy, meetings with different professionals. Patients are registered in the electronic patient registry and we also put family in contact with the other services in their region to ensure continuity of care.

Conclusion: Organizing supportive networks in the community, developing our resource center and exchanging best practices at national and international level improved the access to care for patients with PWS and other rare diseases in Romania.

#2 FAMILY ROLE FOR PEOPLE WITH PWS

▸ **Authors: Alexandru-Tiberiu Dan, volunteer RPWA, reporter Radio NoRo- the voice of patients (RONARD), Alexandra – Loredana Dan, special education teacher at NoRo Center, volunteer at Radio NoRo- the voice of patients (RONARD)**

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Introduction: As a brother of a sister with PWS I had to face different challenges: from thinking that my parents love her more than they loved me to embarassing situation as a small brother.

Methods: We are trying to share with participants some special moments of our life and try to demonstrate that "Love is an important part of the treatment". I was always involved in the RPWA since it was established and since I finished Univeristy I am working as a volunteer for RPWA as a DPO and as a reporter for Radio NoRo – the voice of patients. My wife is a special education teacher and she work at NoRo Center. We meed every day childern with different rare diseases and we learn how important is our family.

Results: growing up in a family that is involved in support activities for patients with PWS and other rare diseases we have the opportunity to learn how to respond in different situations and how to face the everyday challenges while enjoying the life.

Conclusion: Understanding the disease and the barrier that my sister faces every day made me understand the role of our family and friends and how important is to be aware about what you have to do in different situation. It is so important to be „just a brother" and to learn how to be a supportive family member.

#3 PRADER WILLI SYNDROME: SOCIODEMOGRAPHIC CHARACTERISTICS OF FAMILIES AND THE CAREGIVER OVERLOAD

▸ **Deysi Licourt Otero[1*], Anitery Travieso Téllez[1], Soraya Coro Carrasco[2], José Rafael Hernández Gomez[3]**

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Introduction: Early diagnosis of Prader Willi Syndrome is essential for multidisciplinary care. Defining the figure and roles of the caregiver avoids emotional overload, which will result in a higher quality of life for the person and their family.

Objective: To identify the sociodemographic characteristics related to the family and to calculate the degree of overload of the caregiver.

Methods: Was included a universe of 8 families with one member Prader Willi Syndrome in each one, belonging to Pinar del Río Province, Cuba, As instruments of information collection, a sociodemographic survey was applied for families and the test on the burden of the caregiver.

Results: 87.5% of the families are from rural areas, 50% reside in the Consolación del Sur municipality. In two families the caregiver was represented by the grandmother and in the rest by the mothers, in 100% of the latter the dissolution of the marriage was reported, this data was significant in relation to the average cultural level of 11th grade reached between both parents. and the family per capita low.

In the test on the load of the caregiver, a score higher than 56 was obtained, which evidenced intense overload in 62.5% of them.

Conclusions: The mother as caregiver, without coping mechanisms to mitigate overload leads to family instability.

It is essential that measures are taken to improve the quality of life and generate positive coexistence in the family.

#4 THE 'RIPPLE-EFFECT' BENEFITS OF A PWS VOLUNTEER ORGANISATION FOCUSED ON DELIVERING MEMBERS WHAT THEY WANT AND NEED

▸ **Author: Nick Burke, Board Member, Prader-Willi Syndrome Association of Victoria, AUSTRALIA**
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Many of us who have loved-ones with PWS can clearly remember the moment we were told of the diagnosis of this rare and complicated condition. For me the initial emotion was confusion, as I had little idea what PWS was. Moments later when I realised what this meant, I felt fear and isolation and saw doors closing for my child. This was some 13 years ago, and I now see the condition as a part of my daughter's personality more than a condition or disability, although it has each of these other aspects as well.

In this presentation I will discuss the role of a Member Association, in this case PWSA Victoria (a state in Australia) in helping navigate families through the various stages of PWS with examples of services and events the Association organises, how the Association is run and how it ensures it remains relevant to its members. I will talk about how being part of the PWSA Victoria has helped my family and how I have seen it help others.The presentation will include a 4 minute professionally edited video, examples of fund raising and the more significant events and services the Association offers.

PARENTS' CONFERENCE: PROGRAMME

THE CONFERENCE WILL BE HELD IN THE THEATRE

SATURDAY 16TH NOVEMBER

08.30 – 09.00: Registration

09.00 - 09.15: Opening from the Chair
Amalia Balart, Conference chair and Board member of IPWSO, Chile
Tony Holland, President of IPWSO, University of Cambridge, UK
Welcome from our local organisers: Loisel Bello Ulloa and Marlen Román García and their daughter

09.15 - 09.45: Overview of PWS
Dan Driscoll, MD, University of Florida College of Medicine, USA

09.45 – 10.30: The changing face of PWS – progress and the future
Jennifer Miller, MD, University of Florida, USA

10.30 – 11.00: Break

11.00 – 11.30: Chair: James O'Brien, Board member of IPWSO, Australia
Living with PWS / Parents and people with PWS
Amalia Balart, Board member of IPWSO, Chile, Board Member of PWS Association in Chile, Master in Special Education for learning disabilities. Verena Gutmann, Educational Head of Department, Austria

11.30 – 12.30: Essential communication skills for families
Linda Gourash, MD, Pittsburgh Partnership, USA

12.30 – 13.30: Lunch

13.30 – 14.00: Chair: Verena Gutmann, Board member of IPWSO, Austria
Orthopaedic Issues
Harold van Bosse, MD, Shriners Hospital for Children, USA

14.00 – 14.30: Room 1 Theatre - Early development and growth hormone
Chair: Verena Gutmann, Board member of IPWSO, Austria
Children 0 to 18yrs: Constanze Lämmer, Children's Hospital St. Bernward, Germany
Room 2 Vilma Espín - Adolescent and adulthood endocrinology
Chair: Georgina Loughnan, Board member of IPWSO, Australia
Adolescents and adults: Charlotte Höybye, Karolinska University Hospital and Karolinska Institute, Sweden

14.30 – 15.00: Break

15.00 – 16.30: Lectures followed by Workshops
Room 1 Theatre - Children 0 to 12yrs
Chair: Verena Gutmann, Board member of IPWSO, Austria
Healthy start to life: Nutrition: Paulina Bravo, Clinica Santa Maria and Universidad de los Andes, Chile
Physical activity: Daniela Rubin, California State University, Fullerton, USA
Room 2 Vilma Espín - Children 13yrs to adult
Chair: Georgina Loughnan, Board member of IPWSO, Australia
Healthy maturation and lifestyle:
Physical activity: Daniela Rubin, California State University, Fullerton, USA
Nutrition: Paulina Bravo, Clinica Santa Maria and Universidad de los Andes, Chile
Healthy ageing: Susanne Blichfeldt, The Danish Prader Willi Association and Centre for Rare Diseases, Denmark

16.30 – 17.00: Chair: Marguerite Hughes, Vice-President of IPWSO, Ireland
Current research and clinical trials in PWS Jennifer Miller, University of Florida, USA

SUNDAY 17TH NOVEMBER

08.00 – 08.30: Registration

08.45 – 10.00 Lectures then Workshop
Chair: Marguerite Hughes, Vice-President of IPWSO, Ireland
Is it behaviour or a mental health problem?
Tony Holland, University of Cambridge, UK
Janice Forster, Pittsburgh Partnership, USA

10.00 – 10.30: Break

10.30 – 11.00: Chair: Marilyn Dumont-Driscoll, Board member of IPWSO, USA
Developing psychological support strategies to help people with PWS deal with change
Kate Woodcock, University of Birmingham, UK

10.30 – 12.00: Lectures then Workshop
Room 1 Theatre - Children 0 to 16yrs
Chair: Marilyn Dumont-Driscoll, Board member of IPWSO, USA
Early education and school years: Elizabeth Roof, Vanderbilt University, USA
Room 2 Martí – Adolescents to Adults
Chair: James O'Brien, Board member of IPWSO, Australia
Adulthood – work/day program/residential: Hubert Soyer, Regens Wagner Absberg, Germany

12.00 – 12.30: Chair: Marilyn Dumont-Driscoll, Board member of IPWSO, USA
About IPWSO Country Organisations - getting started: Amalia Balart, Board member of IPWSO, Chile

12.30 – 13.30: Lunch

13.30 – 14.00: Chair: Tony Holland, President of IPWSO
Sensory Integration
Janice Forster, Pittsburgh Partnership, USA

14.00 – 14.30: Testimonials: If you are not here...?
Maria Elvira Garcia, Author of The Thief of Smiles and President of the Colombian PWS Association

14.30 – 15.00: Break

15.00 – 15.45: Lectures and open discussion
Emotional Development – Room 1 Theatre
Chair: Georgina Loughnan, Board member of IPWSO, Australia
Speaker: Elizabeth Roof, Vanderbilt University, USA
Room 2 Martí: Social Interaction
Chair: James O'Brien, Board member of IPWSO, Australia
Speaker: Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof, Germany
Room 3 Bolivar Martí: Friendship, Relationships and Sexuality
Chair: Amalia Balart, Board member of IPWSO, Chile
Speaker: Verena Gutmann, Educational Head of Department, Austria

15.45 – 16.15: Questions and Answers from the box and the floor
Chair: Amalia Balart with a panel of speakers

16.15 – 16.30: Close of Conference
Chair: Amalia Balart, Conference chair and Board member of IPWSO, Chile
Speakers: Tony Holland, President of IPWSO and Loisel Bello Ulloa, Representative of Cuban families with PWS

PARENTS' CONFERENCE: SPEAKERS AND MODERATORS

AMALIA BALART, BOARD MEMBER OF IPWSO, CHILE, BOARD MEMBER OF PWS ASSOCIATION IN CHILE, MASTER IN SPECIAL EDUCATION FOR LEARNING DISABILITIES. *ambalart@gmail.com*

Amalia Balart is a Teacher of English and Teacher for Special Needs. She is graduate of Master in Special Education and has worked as Bilingual Therapist to help children with attention deficit disorder, poor executive functions and learning disabilities. She worked for 26 years as Head of Junior at The Newland School in Chile. She is member of the Board of the Chilean PWS National Association and member of IPWSO Board to serve Latinoamerican countries and their PWS communities. She created the Chilean network of families throughout the country, organizing them by zones, each with a Coordinator that reports to the central Board. She is one of the authors of the book "Síndrome Prader-Willi" Guía de Apoyo y Recetas para Celebrar de Manera Saludable". She founded Corporación Señales, a non-profit organization to provide schooling, training and labor oportunities for people with special needs. She is mother of a 38 year old woman with PWS.

SUSANNE BLICHFELDT, MD, THE DANISH PRADER WILLI ASSOCIATION AND CENTRE FOR RARE DISEASES, DENMARK. *s.blichfeldt@dadlnet.dk*

Pediatrician (pediatric neurology, general and developmental pediatrics). Work: more than 30 years of experience with diagnoses and clinical treatment of children with PWS, incl GH treatment at University Hospitals in Denmark. Clinical advisor concerning treatment of adults with PWS. Research: GH treatment of children with PWS. Scandinavian study that led to the general recommendation of GH treatment for children with PWS in Europe in 2000. Presentations and teaching: since 1988 many teaching sessions for caregivers, teachers, parents about PWS in DK, Norway, Sweden, Finland and presentations in England, Ireland, France, Italy, Greenland, Romania and Bulgaria about various subjects in PWS incl living facilities and general medical questions. PWS in DK: Co- founder of the Danish association 1986, since 1990 leader of the advisory board in the association. Publications about PWS leaflets about various subjects, 4x times yearly articles on medical questions in The DK PWS newsletter. IPWSO related: Involved in IPWSO work since it started in 1991. Co-organizer of parent programs for several IPWSO congresses since the first meeting in 1991. IPWSO board member 2001-2004. member of PPBC 2010-2014. Advisor in CSAB since 2004, here we have the last years created our Overview and Evaluation overviews, and we serve as a group as medical advisors for parents and professionals all over the world. Presentations on various medical subjects at the IPWSO conferences especially in the programs for parents and other professionals but also at scientific programs. Associated member of the FAMCARE group as medical advisor. Family: Husband, children and grandchildren, son 39 years old has PWS.

PAULINA BRAVO J., MD, CLINICA SANTA MARIA AND UNIVERSIDAD DE LOS ANDES, CHILE. *paulinabrav@gmail.com*

Paulina Bravo is a medical doctor who is working as a pediatrician at the Pontificia Universidad Católica de Chile. She was awarded the Nutrition Clinical Fellowship at North York General Hospital, Toronto, ON, Canada (2009-2010). Servicio de Pediatría Clinica Santa Maria y Clinica Universidad de los Andes, Santiago, Chile. Red Latinoamericana de Especialistas en SPW

MARILYN DUMONT-DRISCOLL, MD, PHD, BOARD OF IPWSO, USA. *dumonmd@peds.ufl.edu*

Marilyn has a faculty practice with patients with have childhood obesity, PWS, sleep disorders or learning disabilities. A founding member of the Academic Pediatric Association's Continuity Clinic Research Network, the HRSA-funded Genetics Initiative in Primary Care Education Advisory Committee, the APA representative to the March of Dimes Genetics in Practice Initiative, the NIH Secretary's Advisory Committee on Genetic Testing Panel and the Pediatric Academic Societies Executive Committee.

DR. DAN DRISCOLL, MD, PHD, UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE, USA. *driscdj@peds.ufl.edu*

Dr. Driscoll is a Professor of Pediatrics and Genetics, as well as the Hayward Professor of Genetics Research, at the University of Florida College of Medicine. He has been conducting clinical and laboratory research on Prader-Willi syndrome since the late 1980's. He has been a major contributor to the understanding of the genetics of Prader-Willi syndrome (PWS) and genomic imprinting in the PWS region as well as to the elucidation of the natural history of PWS. His group devised the technique (DNA methylation analysis) that is used around the world to diagnose PWS.

Dr. Driscoll is widely published on PWS and a major spokesperson on PWS in the US and internationally. He has had an active PWS clinic for the last 30 years and he was the principal investigator for the PWS component of an NIH funded 12 year national Rare Disease Center grant. He has served on the PWSA (USA) Board of Directors for the last 20 years and is currently the Chair of the Clinical Advisory Board for PWSA (USA), as well as the Chair of the Clinical and Scientific Advisory Board for the International Prader-Willi Syndrome Organization (IPWSO).

JANICE FORSTER, MD, PITTSBURGH PARTNERSHIP, USA. *janiceforstermd@aol.com*

Janice Forster, MD is a developmental neuropsychiatrist from Pittsburgh PA who has been working with children, adolescents, adults with PWS and their families for over 30 years. She has clinical experience with all levels of severity of the syndrome and across all living situations, from family to group home to inpatient hospitalization. Because she has presented across the USA and around the world, Dr Forster has a "world's-eye view" of how PWS is managed. More recently she has become involved in research exploring the developmental phenomenology of PWS and the efficacy of interventions to reduce stress in fathers of adolescents with PWS. She is "one-half" of the Pittsburgh Partnership (www.pittsburghpartnership.com), established 15 years ago with Dr Linda Gourash, for clinical consultation and education of professionals, families, and care givers. In addition to serving on the Clinical and Scientific Advisory Board of IPWSO, Dr Forster is a member of the Clinical Advisory Board of PWSA-USA.

MARIA ELVIRA GARCIA, PRESIDENT OF THE COLOMBIAN PWS ASSOCIATION.
mariaelvira.garciaronderos@gmail.com

Industrial Engineer, mother of four sons, happily married 39 years ago with Mauricio Sánchez, her faithful and inseparable life partner. She worked for 33 years managing companies in different sectors of the economy. From 6 years ago she is dedicated to the care of her youngest son, Carlos Ivan, a 26 year old PWS patient. She wrote the book "The Thief of Smiles, Testimony of a Family with a Special Child," and is president of the PWS Colombian Association.

LINDA GOURASH, MD, PITTSBURGH PARTNERSHIP, USA. *lgourash@icloud.com*

Dr Gourash is board certified as a Developmental and Behavioral Pediatrician. As the Medical Director of the Prader-Willi and Behavioral Disorders Program of the Children's Institute of Pittsburgh she worked for more than 5 years almost exclusively with children and adults with Prader-Willi Syndrome who were referred for inpatient crisis intervention from throughout the USA and Canada. Subsequently Dr Gourash has served on the Board of Directors of the Prader-Willi Syndrome Association of the USA. She is currently providing clinical consultation for the International Prader-Willi Syndrome Organization and the PWSA-USA. She provides consultation and educational programs throughout the US and internationally through Pittsburgh Partnership, Specialists in PWS. (www.pittsburghpartnership.com)

VERENA GUTMANN, BOARD MEMBER OF IPWSO, EDUCATIONAL HEAD OF DEPARTMENT, AUSTRIA. *verena@gutmann.priv.at*

I am from Austria where I developed the Austrian PWS Association and was chairperson for 10 years. I am mother to a 30 year old daughter with PWS. Since 2016 I have been a Board member of IPWSO. I was an Educator and head of the department and responsible for educational management of 100 adolescents. I was asked to focus on puberty issues and organized several talks and workshops. In consequence I conducted lectures and workshops in organizations and colleges for caregiver education: with the focus on "Handicapped sexuality". My main focus now is PWS and sexual issues, gathering more experience, working with PWS caregivers, holding workshops with PWS individuals etc.

NORBERT HÖDEBECK-STUNTEBECK, PHD, DIAKONISCHE STIFTUNG WITTEKINDSHOF, GERMANY. *norbert.hoedebeck-stuntebeck@wittekindshof.de*

Dr. Norbert Hödebeck-Stuntebeck is a Psychologist, Psychotherapist and a Supervisor, who resides in Bad Oeynhausen, Germany, where he currently serves as Projectmanager Prader-Willi-Syndrome and Projektmanager Adipositas (Obesity) for Diakonische Stiftung Wittekindshof (a lutherian foundation in the north west of Germany, in Northrhein-Westfalia). He received his PhD in 2012 at the University of Eichstätt from a study about the competence of people with Prader-Willi-Syndrome (PWS) in change of emotional perspective (empathy). Since 1996 he has been responsible for the development and differentiation of support for people with PWS of all ages and in different fields of living, working, school and training programs. He is the chair of the Professional Providers and Caregivers Board (PPCB) of the International Prader-Willi-Syndrome Organisation (IPWSO) and (co)organizer of all caregiver conferences of IPWSO since the first in Romania in 2007. Since 2015 he has been the CEO of the Prader-Willi-Syndrom Institute Germany (PWS-ID). His interest in research is focused on empathy (change of perspective) in PWS and the development and evaluation of training programs. Another field is the obesity of people with mental handicaps.

PROFESSOR TONY HOLLAND, UNIVERSITY OF CAMBRIDGE, UK. *tonyipwso@gmail.com*

Tony Holland trained in Medicine at University College and University College Hospital, London, qualifying in 1973. After some years in General Medicine he trained in Psychiatry at the Maudsley Hospital and Institute of Psychiatry in London. From 1992 to 2002 he held a University Lecturer's post in the Section of Developmental Psychiatry in the University of Cambridge, and in 2002 was awarded the Health Foundation Chair in Learning (Intellectual) Disability establishing the Cambridge Intellectual and Developmental Disabilities Research Group (www.CIDDRG.org.uk). His specific research interests include the eating, behavioural and mental health problems associated with having Prader Willi Syndrome (PWS); the relationship between Down's syndrome and Alzheimer's disease, and also clinical/legal issues relevant to the needs of people with intellectual disabilities. With colleagues he has published research extensively on these topics in academic and practice-based journals. He works closely with charitable organisations and has been psychiatric advisor to, and Patron of, the UK PWS Association and since 2016 he has been President of IPWSO. In 2010 he was elected a Fellow of the UK Academy of Medical Sciences. In 2015 he was awarded a CBE in the Queen's Birthday Honours for services to psychiatry. Since October 2015 he has held an Emeritus position at the University of Cambridge.

CHARLOTTE HÖYBYE, KAROLINSKA UNIVERSITY HOSPITAL AND KAROLINSKA INSTITUTE, SWEDEN. *charlotte.hoybye@karolinska.se*

Graduated 1986 from Medical School. Certificate as specialist in Internal Medicine 1993 and in Endocrine Diseases 1996. Since 2001 Senior Consultant in Endocrinology, from 2004 to 2017 Head of the Pituitary Section in the department. Since 2010 head of the Expert Group for Treatment of Endocrine and Metabolic Diseases, The Drug and Therapeutic Committee, Stockholm County. Member of the steering committee for the PWS-Clinical Trial Consortium and IPWSO's Clinical & Scientific Advisory Board. PhD 2003 from Karolinska Institute on the thesis "Endocrine and metabolic aspects of adult Prader-Willi syndrome with special emphasis on the effect of growth hormone treatment". Associate professor in Endocrinology, Karolinska Institute 2007.

JENNIFER MILLER, MD, UNIVERSITY OF FLORIDA, USA. *millejl@peds.ufl.edu*

Education: M.D. University of Florida; M.S. Chemistry, Emory University; M.S. Clinical Research, University of Florida. Academic appointments: University of Florida, Department of Pediatrics, Associate Professor. Research focus: My research focuses on investigation of the etiology and possible treatment for hyperphagia and metabolic abnormalities in individuals with Prader-Willi syndrome and individuals with other causes of early-onset obesity. I currently follow over 400 patients with Prader-Willi syndrome from around the world, and over 150 patients with early-onset obesity and the metabolic syndrome. I am currently working on several clinical treatment trials for individuals of all ages who are suffering from Prader-Willi syndrome and early-onset obesity.

ELIZABETH ROOF, VANDERBILT UNIVERSITY, USA. *elizabeth.roof@vanderbilt.edu*

Elizabeth Roof, M.A. is a Research Associate at Vanderbilt University Department of Psychology and has been licensed as a Health Service Provider in TN since 1994. She currently directs several research programs with children and adults with Prader-Willi syndrome with Elisabeth Dykens. They have published many peer reviewed journal articles about many aspects of PWS across lifespan. For almost 25 years, Elizabeth has followed longitudinally over 350 children, teens and adults with PWS in research studies. Elizabeth has recruited many families across the country and Canada by providing individualized feedback information to families on issues such as behavioral and classroom intervention, effective parenting, IEP's and educational strategies, psychiatric medication in PWS, and residential placement and professional consultation for professionals and groups. She has helped manage many clinical trials in PWS and consults with Sponsors to select appropriate outcomes and logistics for Clinical trials in PWS. She has presented at many state and national and International PWS conferences and for FPWR in US, Australia and Canada.

DANIELA RUBIN, PHD, CALIFORNIA STATE UNIVERSITY, FULLERTON, USA. *drubin@fullerton.edu*

Dr Daniela A. Rubin is physical education teacher native of Argentina. In 1999 she moved to the Unites States to purse her graduate studies in the field of exercise physiology at the University of North Carolina Chapel Hill. She is a Professor in the Department of Kinesiology at California State University Fullerton. Her interest in the topic of exercise endocrinology, inflammation and obesity led to several projects comparing hormonal, metabolic, and inflammatory responses to exercise in children, including youth with Prader-Willi Syndrome (PWS). As she became more involved in understanding the challenges faced by people with PWS, her studies sought to examine exercise aspects in this syndrome from a multidimensional perspective. Her studies characterized physical activity patters using accelerometry, examined motor aspects in terms of sensory reception and integration and motor proficiency, cardiorespiratory responses to exercise, energy expenditure, body composition and phenotype. Her team also developed and tested a 24 weeks physical activity intervention in 116 children with and without PWS (Active Play at Home©, FunDoRoo©). Using a game-based approach parents completed an at-home routine with their children showing improvements in motor proficiency, health-related quality of life and inflammatory and metabolic factors. Her last intervention study involved children ages 4-7 doing physical activity with their parents. She has served as a board member in the Prader-Willi California Foundation since 2013.

HUBERT SOYER, REGENS WAGNER ABSBERG, GERMANY. *hubert.soyer@regens-wagner.de*

Ph.D., Psychology and Pedagogics, Catholic University of Eichstätt-Ingolstadt, 2003. Dissertation: Studies on social and therapeutic pedagogy of Prader-Willi Syndrome. Diploma: Psychology, Catholic University of Eichstätt-Ingolstadt, 1999. Teaching profession for Primary and Secondary School and Special Education School, 1977. Associate lecturer at the Chair for Social Education at the Catholic University of Eichstätt-Ingolstadt since 1999. General Manager of Regens Wagner Absberg since 1994. Regens Wagner Absberg is an institution for adult handicapped people offering facilities for living and working. For 20 years the institution has offered a special treatment for people with Prader-Willi Syndrome. Since this time there is cooperation with the Zentrum für Neuropsychologie – Trier and the Catholic University of Eichstätt-Ingolstadt for research on the subject of Prader-Willi Syndrome. IPWSO Board: Co-opted Board member, June 2011. Professional Providers & Caregivers' Advisory Board: Board member. Organizer of the International PPCB Conferences 2018 in Munic, 2012 in Wildbad Kreuth, 2009 and 2008 in Herne, Germany together with Dr. Norbert Hödebeck-Stuntebeck and the Board members of PPCB. Managing director in the newly established non-profit company Prader-Willi-Syndrom Institut Deutschland gGmbH (PWS-ID).

HAROLD VAN BOSSE, SHRINERS HOSPITAL FOR CHILDREN, USA. *HvanBosse@Shrinenet.org*

Harold J.P. van Bosse, M.D. has been practicing pediatric orthopaedic surgery exclusively since completing his orthopaedic residency at the University of Illinois in Chicago in 1994, and his fellowship at Toronto's Hospital for Sick Children in 1995. He joined the staff of the Philadelphia's Shriners Hospital for Children in 2008, allowing for a more focused practice treating conditions of special interest. His interest in Prader-Willi syndrome developed from treating a 2 year old child with PWS and severe scoliosis. Through that patient, Dr. van Bosse was introduced to the community of specialists caring for children with PWS, joining them to round out the comprehensive care of these challenging and rewarding patients. Much of his efforts have been treating the very young child with PWS and spine deformities. For these children, treatment devoted to the least invasive modalities that will preserve spinal growth and chest development. These include bracing, spinal casting and expandable implants, to avoid a spinal fusion during childhood. Dr. van Bosse is a member of the Clinical and Scientific Advisory Board of IPWSO, the Clinical Advisory Board of PWSA-USA, and has given talks on the orthopaedics of PWS at PWSA-USA, FPWR, PWANY and PWCF meetings over the years.

KATE WOODCOCK, UNIVERSITY OF BIRMINGHAM, UK . *K.A.Woodcock@bham.ac.uk*

Dr Kate Anne Woodcock is a Senior Lecturer at the Centre for Applied Psychology in the School of Psychology at the University of Birmingham, UK. Her research focuses on young people who face psychological and behavioural difficulties, often those linked to neurodevelopmental disorder. Several lines of her research focus specifically on individuals with Prader-Willi syndrome. Kate's work has examined factors that come together to precipitate behaviours that can be challenging for individuals with Prader-Willi syndrome, such as temper outbursts. Her team is currently engaged in work that applies this knowledge to the development of intervention strategies. For example, caregiver led behavioural support strategies, cognitive training intervention programmes, and early intervention strategies. Kate carried out her PhD research at the University of Birmingham between 2005 and 2008.

Two years of her Postdoctoral Research were at Peking University, China between 2011 and 2013. Kate held a lectureship position at the School of Psychology, Queen's University Belfast between 2014 and August 2017.

PARENTS' CONFERENCE: SPEAKER ABSTRACTS

SATURDAY 16TH NOVEMBER

OVERVIEW OF PWS

▸ Professor Dan Driscoll, MD, PhD, University of Florida College of Medicine, USA

Prader-Willi Syndrome (PWS) is a complex neuroendocrine contiguous gene syndrome. The clinical features, natural history and the genetics will be reviewed.

THE CHANGING FACE OF PWS – PROGRESS AND THE FUTURE

▸ Jennifer Miller, University of Florida, USA

This talk will focus on medications, therapies, and supplements which have helped change the lives of individuals with Prader-Willi syndrome. Dr. Miller will discuss growth hormone treatment, other medications which have been used in some patients (oxytocin, pitolisant), as well as physical therapy and ABA therapy, and a variety of supplements which have been tried in some patients with PWS. Lastly, Dr. Miller will discuss future potential treatment options for individuals with PWS and potential impact of research on the future for individuals with PWS.

LIVING WITH PWS / PARENTS AND PEOPLE WITH PWS

▸ Amalia Balart

Board member of IPWSO, Chile, Board Member of PWS Association in Chile, Master in Special Educations for learning disabilities. Verena Gutmann, Board member of IPWSO, Educational Head of Department, Austria.

In this session you will learn about the journey a family takes on, when living with their adult children with PWS. We will be discussing fears, happy moments, accomplishments and failures and how day by day, we try to overcome adversity to provide a life full of meaning for our loved ones.

We hope to assist families, by pointing some of the most relevant issues and needs ofpeople with PWS staying with us, to ensure good health, life enjoyment and most well adapted behaviour possible.

ESSENTIAL COMMUNICATION SKILLS FOR FAMILIES

▸ Linda Gourash, MD, Pittsburgh Partnership, USA

Persons with PWS are prone to disruptive behaviors when they are faced with either uncertainty or disappointment. Managing their expectations as well as their anxiety is key to managing their behavior. In this talk Dr Gourash will delineate in detail the skills needed by families and other caregivers for effective communication with persons with PWS. Common causes of discord among family members and useful solutions will be highlighted. Handout in English and Spanish.

ORTHOPAEDIC ISSUES

▸ Harold van Bosse, Shriners Hospital for Children, USA

Children with Prader-Willi syndrome have a number of important orthopaedic issues. Milestones can take twice as long, and the children may need extra help achieving them, including bracing and physical therapy. Children with PWS may have decreased bone strength, making them susceptible to fractures. Other concerns for both the infant/toddler and in the older child are scoliosis, hip dysplasia and flatfootedness. In this presentation, we will discuss various options for helping children with PWS gain muscle and bone strength. We will examine strategies for monitoring of spine and hip problems. Focusing on the spinal deformities, we will outline a treatment process, including bracing, spinal casting, expandable spinal implants and spinal fusion. We will also discuss anaesthetic and post-operative recovery concerns for children with PWS undergoing surgery. The presentation will be in slide show format, and questions will be answered at the end of the session, time permitting.

EARLY DEVELOPMENT AND GROWTH HORMONE: CHILDREN 0 TO 18YRS

▸ Constanze Lämmer, Children's Hospital St. Bernward, Germany

Prader-Willi Syndrome is a complex neurogenetic disorder. The holistic treatment concept includes nutrition, sports and movement and behavioral management. In the year 2000 Growth hormone treatment in Children with genetically confirmed Prader-Willi-syndrome was approved. Growth hormone gains an important place in the treatment concept for children with PWS. In many countries Growth hormone treatment starts in the first year of life. Contra indications, especially sleep apnea and heart problems have to be checked before. Growth hormone improves body composition and increases final height. Due to increased muscle mass children crawl and walk independently earlier than without Growth hormone. They are able to interact with peers and environment earlier. They make positive moving experience, are more active, gain more muscles and have fun at sport. This makes weight management easier. The more intensive interaction with the environment has also a positive impact on cognitive function. During Growth hormone therapy monitoring of the clinical situation, the hormone values and metabolic situation, cardiac function, sleep and orthopedic situation have to be checked on a 3 to 6 months basis. Growth hormone treatment has to be finished if final height is reached.

ADOLESCENT AND ADULTHOOD ENDOCRINOLOGY

▸ Charlotte Höybye, Karolinska University Hospital and Karolinska Institute, Sweden

Many symptoms in Prader-Willi syndrome (PWS) are similar to symptoms caused by insufficient hormone levels. In this presentation symptoms and treatment of growth hormone deficiency, central adrenal insufficiency, central hypothyroidism and hypogonadism in adolescents and adults with PWS will be discussed. Decreased growth rate, muscular hypotonia, abnormal body composition and impaired quality of life are well-known symptoms of growth hormone deficiency (GHD). Studies have shown that GHD is not present in every child and adult with PWS, but other studies have consistently shown significant benefits of GH therapy on growth, body composition, physical and psycho-social function. GH doses in adolescents are higher than in adults. Adrenal insufficiency is characterised by fatigue, weight loss and insufficient response to stress and central adrenal insufficiency was hypothesized to be responsible for sudden deaths in PWS. However, most studies indicate that low levels of cortisol are rare, and evaluation and treatment rarely indicated. Increase in weight, fatigue, and low body temperature are characteristics of hypothyroidism. Central hypothyroidism has been reported with a high frequency in children but not in adults. Due to similarities with symptoms in PWS regular follow-up of thyroid function is recommended.

Sex hormones are important for appearance of body gender, body composition, bone mineral density, fertility and quality of life. Low levels of sex hormones, which are oestrogen in women and testosterone in men, are very common in PWS, most often due to insufficient function of testes or ovaries. Sex hormone treatment is not feasible for all and there is no consensus on treatment. Therefore, an individual consideration of benefits and risks is recommended. Five pregnancies have been described in PWS women. Fertility in PWS males has not been reported. Some symptoms in PWS share similarities with hormone insufficiencies. As some of the hormone insufficiencies are common, diagnosis and hormone replacements are important along with prevention of obesity and treatment of comorbidities for optimal care in adults with PWS. Special considerations are needed during the transition phase.

NUTRITION

▸ Paulina Bravo, Clinica Santa Maria and Universidad de los Andes, Chile

Nutrition through Prader-Willi life from newborn to school age: This talk will incorporate a review of the nutritional phases during pediatric life and applied to daily life.Nutrition through Prader-Willi life from puberty to adulthood: This talk will include information about practical nutritional aspects through puberty to adulthood.

PHYSICAL ACTIVITY: READY TO MOVE AND HAVE FUN? MAKING PHYSICAL ACTIVITY AN ESSENTIAL PART OF DAILY LIFE

▸ Daniela Rubin, PhD, California State University, Fullerton, USA

Movement, physical activity, and exercise are all essential to all persons but especially important for those people with Prader-Willi Syndrome. Movement in people with PWS not only contributes to maintaining a healthy weight, but is also important for social interaction, sense of self, and overall quality of life. This session will present recommendations of activities for young and older children, adolescents and adults. For young and older children movement will be presented through games that help build physical skills such as balance, coordination, agility and strength. In adolescents and adults, physical activity recommendations will include not only walking but also strengthening exercises as well as exercises to help with balance and why are these so important. The session will provide practical examples of how to build a physical activity routine and highlight some key exercises to include in the routine and how to make it fun.

HEALTHY AGEING

▸ Susanne Blichfeldt, MD, The Danish Prader Willi Association and Centre for Rare Diseases, Denmark

Introduction: Thanks to growing knowledge, treatment possibilities and care, persons with PWS now survives into adult age and many are living healthy and happy lives, and are facing the possibility of becoming old and needing extra support as other older people do.

Background: Still we do not have large population studies about aging and health in adults with PWS, but many case reports tell about people in their 60-70 ties, being healthy and not overweight thanks to ongoing support. As adults (PWS) do not have a normal sensation of satiety, always like to eat but have lower than normal calorie needs, they will become severely obese without needed support. With obesity follows diseases which in PWS adults typically are respiratory and circulatory problems, hypertension, leg edema, leg ulcers and also type 2 diabetes. Other complaints can be joint problems and limitation of physical activity, which again can worsen the circulatory problems. Beside the ongoing risk of overweight in PWS there are special health problems in adults related to PWS itself: hormonal deficiency, osteoporosis, obstipation and psychiatric diseases such as depression and psychoses, and correct treatment here is of utmost importantance. Also the very special PWS related behavioral traits, which can be misinterpreted as psychiatric disease must be known. Risk of choking, stomach perforation, temperature instability, lack of fever with infections and high pain threshold are also situations met in adults.

Methods: Recommended yearly medical visits and blood tests are recommended for all adults (PWS). As access to medical support and knowledge about PWS varies a lot among countries the CSAB has published on the IPWSO web site Overview and Evaluation Guidance concerning adults (PWS), to be downloaded: www.IPWSO.com/medical-professionals meant for both professionals and families. Also planned daily routines with meaningful occupation and physical activities as walking one hour per day is recommended for all.

Conclusion: Healthy aging in PWS is possible, but much support based on individual needs is necessary. Ongoing control of weight and food together with daily planned physical activity and regular medical evaluation are essential.

CURRENT RESEARCH AND CLINICAL TRIALS IN PWS

▸ Jennifer Miller, University of Florida, USA

Dr Miller will discuss all of the current clinical trials being done for individuals with PWS. The focus of this talk will be the indications for each of the clinical trials, treatment intent, and things to be aware of with each clinical trial. She will discuss the problems we have encountered with research trials, as well as the benefits of the trials.

SUNDAY 17TH NOVEMBER

IS IT BEHAVIOUR OR A MENTAL HEALTH PROBLEM?

▸ Tony Holland, University of Cambridge, UK

▸ Janice Forster, Pittsburgh Partnership, USA

The occurrence of problem behaviours and the development of mental illness are common in people with Prader-Willi Syndrome (PWS), and both impact negatively on the person's quality of life and that of their families. The focus of this workshop will be: how best to identify and understand the reasons for typical problem behaviours, and how to recognize and distinguish them from symptoms of mental illness. The most common behaviors associated with PWS will be presented, and the transition to the development of a secondary mental illness will be described. Specific attention will be given to contributing factors such as age, environment, stress, and genetics. Based on the understanding of these factors, interventions that may help to prevent and manage problems will be discussed (the PWS Intervention Pyramid). The potential benefits and risks of psychiatric medications will be considered.

PWS INTERVENTION PYRAMID

Those attending the workshop will be encouraged to bring their experiences for consideration. The workshop will take the form of brief presentations and more extensive discussion, bringing together the experience and expertise of all who are present.

DEVELOPING PSYCHOLOGICAL SUPPORT STRATEGIES TO HELP PEOPLE WITH PWS DEAL WITH CHANGE

▸ Dr Kate Anne Woodcock, University of Birmingham, UK

People with PWS often find changes to their expectations extremely difficult. These changes cause upset and anxiety and can trigger temper outbursts. Our research has described pathways that lead people with PWS to show such resistance to change, which include atypical brain function and thoughts (cognitive skills). I will discuss helping strategies that we have developed and are currently testing, which target specific steps in these pathways to try to reduce difficulties with change. One of the helping strategies uses an internet based tablet or mobile computer game. We designed the game in collaboration with PWS families to train the cognitive processes that are important for coping with change effectively. Another helping strategy uses an internet based system to support families to create the kind of environment for their young children, which we think will support the development of the cognitive skills that are needed to cope effectively with change.

DESAROLLO DE ESTRATEGIAS DE APOYO PSICOLÓGICO PARA AYUDAR A LAS PERSONAS CON SPW A SOBRELLEVAR LOS CAMBIOS

Las personas con SPW tienden a tener dificultades con los cambios imprevistos, que suelen causarles malestar y ansiedad y pueden desencadenar crisis emocionales. Nuestra investigación nos ha permitido explicar las secuencias que llevan a las personas con SPW a experimentar resistencia a los cambios. Esas secuencias incluyen funciones cognitivas y del cerebro. Hemos desarrollado técnicas que se enfocan en algunos de los pasos de esas secuencias y sirven para reducir los problemas causados por los cambios. Actualmente estamos evaluando el desempeño de esas técnicas. En mi presentacion, voy a explicar algunas de ellas.

Una de las técnicas incluye un videojuego que hemos desarrollado en colaboración con familias PW. El videojuego sirve para entrenar los procesos cognitivos que una persona necesita para poder tolerar bien los cambios inesperados. Otra de nuestras técnicas se basa en un sistema accesible por internet que le facilita a las familias crear la clase de ambiente en el cual los niños pequeños pueden desarollar esas habilidades cognitivas indispensables para poder tolerar cambios.

EARLY EDUCATION AND SCHOOL YEARS

▸ Elizabeth Roof, Vanderbilt University, USA

Does the use of growth hormone, physical therapy and occupational and speech therapy in very young children with PWS change their school readiness and their ability to learn? There are some things that parents can help to make sure their child gets the best start in school and is able to take part in classroom activities with other students. Teaching skills like turn taking, cooperation, natural consequences, and positive reinforcement can help get children with PWS ready to get the most out of a classroom. Getting early evaluations to paint an accurate picture of strengths and weaknesses and then using that information to build your child's school team can go a long way to combat some of the negative personality characteristics of PWS: stubbornness, rigidity, anxiety and inattention. We will talk about how to communicate effectively with your teachers and the school staff to help get the support your child needs without alienating anyone. We will talk about to develop realistic goals for your child and his school staff, when (and HOW) to fight for what your child needs in the classroom. Make sure your child has the best fit in teachers and what warning signs to look for in your child's school staff. This will be very hands on and interactive presentation.

ADULTHOOD – WORK/DAY PROGRAM/RESIDENTIAL

▸ Hubert Soyer, Regens Wagner Absberg, Germany

The workshop presents examples of different living arrangements for PWS people. There is consensus that adequate support in housing must include food security (eg nutritional plans), weight control, a structured daily schedule of meaningful employment, exercise programs, recreational opportunities, and adequate recreational activities by trained caregivers. Finding the balance between control and self-determination is the challenge of achieving the highest quality of life.

Work is an essential part of life and it should be different just like every individual. Many people with PWS are struggling in their current work environment or from the absence of it. Work environments are often not conductive, educated, or willing to support the specialized needs of PWS. There are important reasons to provide work opportunities to people with PWS. First of all it gives them self-esteem and the feeling of being needed. For them it's not only about earning their own money and feeling more independent, but also about finding themselves integrated in the common social structures. Furthermore, work gives them a structured daily routine and the security they need. It improves their empowerment as well as their social contacts. Therefore, an adapted environment is absolutely imperative.

ABOUT IPWSO COUNTRY ORGANISATIONS - GETTING STARTED

▸ Amalia Balart, Board member of IPWSO, Chile

This presentation will provide an overview of the importance to have a group of parents well organised, and the various tasks to be done to become an association with a legal structure, membership and statutes. It will review main procedures to be carried out and objectives to be achieved, in order to create a strong support group of professionals and parents. It will emphasize the necessity of having a proactive Board, well conformed and with a clear mission. It will focus on the many opportunities to develop for the wellbeing of the people with PWS in your community, highlighting the risks that a new organisation may encounter during the starting process and will provide ways of ensuring successful outcomes.

SENSORY INTEGRATION: SENSORIMOTOR ISSUES IN PWS

▸ Janice L. Forster, MD, Pittsburgh Partnership, USA

Hypotonia (low muscle tone) is one of the characteristic symptoms related to the diagnosis of PWS. It affects critical developmental stages in infancy (attachment, feeding, imitation, exploration). It has an impact on brain maturation (low arousal, impaired empathy/theory of mind, visual perceptual motor and speech delay) and body function (stamina, gastrointestinal motility, urinary problems, breathing difficulties, and problems with balance and truncal posture). In addition to hypotonia, information processing of sensory experience is deficient in PWS in both the peripheral and central nervous system. These intrinsic deficits result in sensory deprivation that results in a condition of sensory hunger for the brain in PWS. Sensory hunger leads to behaviors are commonly associated with the syndrome, such as stereotypic (habit) behaviors, skin picking, and excessive/repetitive experiences with water, soap, lotions, shampoo, etc. Sensory hunger also results in body exploration that can develop into behavioral patterns of nose, anal and vaginal picking. Management of sensory hunger in PWS is essential to improve adaptive function. Assessment of each individual's sensory needs is necessary, usually by an occupational therapist. Through the regular implementation of prescribed activities, sensory hunger can be satisfied resulting in improved adaptive behavior in persons with PWS at all ages.

TESTIMONIALS: IF YOU ARE NOT HERE...?

▸ Maria Elvira Garcia, Author of The Thief of Smiles and President of the Colombian PWS Association

An approach to those moments when we cannot be next to our children with PWS, either because we get sick, die or just decide to go to vacation.

If you are not here:

1. How prepared is our closest family circle, our partner and themselves to continue with a calm and happy existence?
2. How have we taught them to face the partial and definitive absences of their loved ones?
3. Do we know what their brothers think and feel about the idea of taking care of them when we can no longer do it?

Transcending in our daily activities of caregivers to reach the spiritual level, that in which no soul knows of disability and we are all equal, may be is the most important legacy for our children and family.

"Y CUÁNDO FALTES...?"

Una mirada hacia esos momentos en que no podremos estar al lado de nuestros hijos con SPW, bien sea porque enfermemos, fallezcamos o simplemente nos tomemos la libertad de unas vacaciones.

Y cuando faltes:

- ¿Qué tan preparados está nuestro círculo familiar más cercano, nuestra pareja y ellos mismos para continuar con una existencia tranquila y feliz?
- ¿Cómo le hemos enseñado a nuestros hijos a afrontar las ausencias parciales y definitivas de sus seres amados?
- ¿Sabemos qué piensan y sienten sus hermanos frente a la idea de hacerse cargo de ellos cuando nosotros ya no podamos hacerlo?

Trascender en nuestras actividades cotidianas de cuidadores para llegar al plano espiritual, ese en el que ninguna alma sabe de discapacidad y todos somos iguales, tal vez pueda ser el legado más importante para nuestros hijos y familia.

EMOTIONAL DEVELOPMENT

▸ Elizabeth Roof, Vanderbilt University, USA

There is little known about emotional development in Prader-Willi Syndrome, though delays are noted- do they continue throughout lifespan? How can we identify these weaknesses and strengths in PWS? Are there ways to help children and teens with PWS catch up to their peers? Although many persons with PWS have problems in thinking, mood and social interactions, most do not meet formal criteria for ASD, psychosis, or other psychiatric disorders. Even so, studies to date on psychopathology in PWS rely primarily on psychiatric diagnoses, and these labels differ considerably across countries, clinical perspectives, labs, and disciplines (i.e., ICD-10, DSM-IV, adapted systems). Making reliable psychiatric diagnoses is also challenging in people with intellectual disabilities in general (Dykens, 2000), which further clouds diagnoses in PWS. It is important to determine what other co-morbid diagnoses may be contributing to delays in emotional development in those with PWS.

What do we know about recognition of emotional states in children and adults with PWS? Do they notice the cues that play into emotional starts in others- facial expression, voice timbre and words and other body gestures that help us identify how someone is feeling? We evaluated over 125 children and adults with PWs and asked them to name the feeling on a standardized emotional recognition task and asked them to name emotions like fear, anger, happy, sad, contempt, and surprise. We found that there were some significant weaknesses in this task and that they often ignored important cues. We also asked to watch short video clips of children in different social situations and could they read direct and indirect forms of communication and did the skills get better as those with PWs aged?

We have some interesting data to present and will talk about subtype differences, and what types of things parents, teachers and therapists can offer to help develop emotional recognition and how that plays into social skills and friendships. We will also talk about how certain interventions can be used across settings and seem to hold a great deal of promise in emotional development and social skills in those with PWS.

SOCIAL INTERACTION

▸ Norbert Hödebeck-Stuntebeck, Diakonische Stiftung Wittekindshof , Germany

People with Prader-Willi-Syndrome are in contact (in social interaction) with so many people in different settings: in the family, in school, at work in their leisure time and at other places - very similar to our own situation. Most of us handle these social situations (communication) with others in a more or less successful way, so that we have friends, relationships and partnerships over many years. The presentation focus on some of the main problematic backgrounds (symptoms) of the Prader-Willi-Syndrome which are responsible for many of the all-day stressful situations for people with PWS in social interaction. But also the presentation will inform about ways in which we can support the development of competences so that people with PWS will be more able to handle this social situations / the social interaction in a more and more adequate way by themselves.

FRIENDSHIP, RELATIONSHIPS AND SEXUALITY

▸ Verena Gutmann, Educational Head of Department, Austria

As we know the sexual development of PWS individuals is diminished (hypogonadism - one of the main symptoms of PWS) but the emotional possibilities, the desire for a sexual or marriageable relationship is quite normal. Sexual maturity does not fully develop. Does that mean that we don't need to speak and to discuss the issues connected with their emotional life? "Fertility in PWS raises many medical and ethical issues and appropriate anticipatory guidance, counselling and education are important." (Clinical Scientific Advisory Board-IPWSO, 2019)

We are challenged to help them to find their special identity. We will speak and discuss topics and questions like:

1. Knowledge: What is different with PWS?
2. Encouragement of social skills
3. Self-determined relationship and sexuality for people with PWS?

Let us focus on a really important and essential issue for the quality of life with PWS, beside "hunger and satiety".

PROGRAMME FOR PEOPLE WITH PWS: 16TH TO 17TH NOVEMBER

ACTIVITIES WILL BE HELD IN THE COMPLEJO EL LIBERTADOR AND RUN FROM 08.00 TO 17.00 OVER THE SATURDAY AND SUNDAY OF THE CONFERENCE. FINAL SCHEDULES WILL BE GIVEN TO FAMILIES DIRECTLY.

	PREESCOLAR (N=7)		ESCOLAR (N=7)	
HORA	**ACTIVIDAD**	**SALA**	**ACTIVIDAD**	**SALA**
SÁBADO				
8:00-9:00	Bienvenida	Sala C	Bienvenida	Sala C
9:00-10:00	Juegos activos	Patio	Juegos activos	Patio
10:00-10:30	Snack	Patio	Snack	Patio
10:30-11:30	Cuentacuentos, canciones	Teatro	Juegos mesa	Sala A
11:30-12:00	Colorear	Sala C		
12:00-1:00	Almuerzo	Patio	Almuerzo	Patio
1:00-2:00	Siesta / Manualidades	Sala C	Manualidades	Sala C
2:00-2:30	Baile	Sala C	Baile	Sala C
2:30-3:00	Snack	Sala C	Snack	Sala C
3:00-4:30	Película / Pasatiempos	Teatro / Sala C	Película / Pasatiempos	Teatro / Sala C
4:30-5:00	Colorear	Sala C	Juegos mesa	Sala C
DOMINGO				
8:00-9:00	Bienvenida	Sala C	Bienvenida	Sala C
9:00-10:00	Cuentacuentos, canciones	Teatro	Juegos activos	Patio
10:00-10:30	Snack	Teatro	Snack	Patio
10:30-11:00	Juegos activos	Patio	Equilibrios	Sala A
11:00-11:30				
11:30-12:00			Bingo	Teatro
12:00-1:00	Almuerzo	Patio	Almuerzo	Patio
1:00-1:30	Siesta	Sala C	Pasatiempos	Sala A
1:30-2:00	Manualidades	Sala C	Juegos tradicionales	Patio
2:00-2:30				
2:30-3:00	Snack	Sala C	Snack	Sala C
3:00-4:30	Película / Pasatiempos	Teatro / Sala C	Película / Pasatiempos	Teatro / Sala C
4:30-5:00	Colorear	Sala C	Juegos mesa	Sala C

	JÓVENES (N=11)		ADULTOS (N=11)	
HORA	**ACTIVIDAD**	**SALA**	**ACTIVIDAD**	**SALA**
SABADO				
8:00-9:00	Bienvenida	Sala A	Bienvenida	Sala A
9:00-10:00	Manualidades	Sala C	Equilibrios	Sala A
10:00-10:30	Snack	Sala C	Snack	Sala A
10:30-11:30	Baile Bingo	Patio Teatro	Manualidades	Sala C
11:30-12:00				Patio
12:00-1:00	Almuerzo	Patio	Almuerzo	
1:00-2:30	Pasatiempos Juegos activos	Sala A Patio	Baile Relajación	Patio Teatro
2:30-3:00	Snack	Patio	Snack	Patio
3:00-4:30	Película / Pasatiempos	Teatro / Sala C	Película / Pasatiempos	Teatro / Sala C
4:30-5:00	Mi diario	Sala A	Mi diario	Sala A
DOMINGO				
8:00-9:00	Bienvenida	Sala A	Bienvenida	Sala A
9:00-10:00	Equilibrios	Sala A	Juegos activos	Patio
10:00-10:30	Snack	Sala A	Snack	Patio
10:30-11:30	Juegos tradicionales	Patio	Bingo	Sala C
11:30 - 12:00			Pasatiempos	Sala C
12:00-1:00	Almuerzo	Patio	Almuerzo	Patio
1:00-1:30	Juegos mesa	Sala A/		
1:30-2:00	Relajación	Teatro	Juegos tradicionales	Patio
2:00-2:30				
2:30-3:00	Snack	Patio	Snack	Patio
3:00-4:30	Película/ Pasatiempos	Teatro / Sala C	Película / Pasatiempos	Teatro / Sala C
4:30-5:00	Mi diario	Sala A	Mi diario	Sala A

IPWSO TRAVEL SCHOLARSHIPS 2019

This year we have been delighted to be able to award the following 10 people with IPWSO travel scholarships to the 10th IPWSO International Conference in Cuba. There were 31 applications.

JUAN CARLOS REYNA
(MEXICO) PROFESSIONAL
I work at Fundación Mara Jose foundation allied with IPWSO

JORGE ESTANISLAO (PERU) PROFESSIONAL
I am a clinical geneticist and I want to create a multidisciplinary team in Peru to help people with PWS

MOLELEKENG SETHUNTSA
(SOUTH AFRICA) PROFESSIONAL
I am a clinical psychologist with an interest in genetic disorders.

NIKOLINKA YORDANOVA
(BULGARIA) PROFESSIONAL
I am a last year resident medical doctor in Pediatric Endocrinology Department and first year PhD student.

DENITSA DIMITROVA
(BULGARIA) PARENT
We have an Association which has not been active for a while; we are bringing this back to life.

MARIO ARNOLDO MENDEZ
(EL SALVADOR) PARENT
I am a psychologist and my wife is an educator. Our son is 27.

MARIA ELVIRA GARCIA RONDEROS
(COLOMBIA) PARENT
I'm the president of the Colombian Prader Willi Association

SANDRA COSTI
(ARGENTINA) PARENT
I am currently the President of the Asociación Argentina SPW

ANIL CHOUBEY
(INDIA) PARENT
Chair of PWSA India and past IPWSO board member

ZURAB ABJANDADZE
(GEORGIA) PARENT
Member of Georgian PWS Association, our son with PWS is 3 years old.

THANK YOU TO LINDA THORNTON

As 2019 comes to a close, our dear friend, Linda Thornton, will take a few steps away from IPWSO as she retires from her role running the day to day work of the organisation. Linda is known to many people within the world of PWS, but most people may not know the extent of her passionate and tireless commitment to IPWSO.

She established the New Zealand PWS Association in 1989 and remained the National Director until 2011. She received the Queen's Service Medal in 1999 for her work with PWS in New Zealand. Linda is a founding member of IPWSO, and has held a significant role on the Board of Directors since its inception in May 1991, at the 1st International PWS Conference held in Noordwijkerkout, The Netherlands.

IPWSO is made up of people from across the globe, many of whom became involved as a direct result of Linda's encouragement and nurturing. In 1992 she initiated and continued to edit, Wavelength, the IPWSO Newsletter for parents and other interested associates of PWS, or better described as "the mouthpiece for everyone involved in the management of PWS". This was expanded to include a scientific section in 1995, with 2 publications completed each year.

In 1999 she completed a Winston Churchill Memorial Trust Fellowship scholarship dedicated to the research the best practices of residential care for people with PWS. She has spoken on PWS around the world to conference audiences, family groups and individuals and has been responsible for numerous publications on PWS, in either hard copy or virtual articles. Her booklet, PWS and the Younger child, first published in 1996, has been the "go to" survival kit for most new parents. It has been updated and reprinted 4 times. Then of course are her wonderfully diverse IPWSO blogs, either written by or sourced by Linda!

She was responsible for bringing the world of PWS 'down-under' to Christchurch, New Zealand for a most successful and memorable 5th IPWSO Conference and 9th Australasian Conference, in 2004, after which, at Linda's suggestion, Asian Pacific Conferences were commenced. Linda has been integral to the success of most of the IPWSO conferences, either as a member of the organising committee or behind the scenes coordinating speakers, programmes, written material, registration or public relations.

Linda has single-handedly managed the fabulous IPWSO website since such a thing was possible. This has been a mammoth task that she has executed as expertly and as smoothly as any professional webmaster. She has steered consecutive IPWSO Boards with her knowledge and experience and never wavered from suggesting, speaking out or objecting to anything she felt was important to the wellbeing of people with PWS. She has been a most valuable member of Famcare, and helped to write all the Famcare articles.

Perhaps her most memorable role, however, will be that of a "people person". Linda has reached out to so many parents of children with PWS from all over the world, in a way only a loving, understanding, passionate and dedicated parent of someone with PWS, can do. She has nurtured and supported their difficult and good times, long before the internet made communication so much easier. She has shared her knowledge and personal experiences with families and professionals and never been afraid to stand up for the person with PWS. In the words of others, Linda has been described as: supporting and welcoming; processing verbal excellence; an exceptional person with great talent who transmits knowledge with a great heart and much humor; integral to the success of IPWSO; my role model, my ideal, my guide; a great partner to work with; full of humor and empathy; wise words; tenacious; driven; inspirational; a most gentle powerhouse and sheer delight to know.

She has been and I imagine always will be, a true ambassador for people with PWS. It was Linda who taught us all to use the phrase "people with PWS" rather than the label, "Prader-Willis". Linda's dedication and commitment to IPWSO, has made an enormous difference to so many people around the world - parents, family members, professionals and most importantly, people with PWS. We wish her the very best for her new role of a "retired lady". You might be able to remove the lady from IPWSO but I doubt you can completely remove IPWSO from the lady!

Linda will be greatly missed but always remembered.

Written by Georgina Loughnan on behalf of the President and Board of IPWSO and all your hundreds of IPWSO friends around the world!

THE IPWSO SONG:
TO SING ALONG WITH AT THE GALA

Fly High

We come here together
to meet with each other,
to share our life stories,
to tell of our glories
sometimes it's not easy
to always be different,
but you are my friend here
and you understand me.

Across the world's oceans,
across the world's skies
we join hands together
and love makes us fly high!

We're brothers, we're sisters,
we're part of the family
that binds us together
from heartland to city.
Like droplets of rainfall
we flow like a river,
combining our wisdom
like powerful seas...

Across the world's oceans,
across the world's skies
we join hands together
and love makes us fly high!

So let us stand tall now,
let's stand tall with pride.
Let's celebrate life now,
both your life and mine
we stand on the same side.
Though we live apart,
just knowing you're there friend,
stays deep in my heart...

Across the world's oceans,
across the world's skies
we join hands together
and love makes us fly high!

Vuela alto

Venimos juntos
aquí a reunirnos,
narrar nuestra historia,
hablar de las glorias;
aunque no es fácil
ser siempre diferente
pero tú amigo
me quieres, me entiendes...

A través de los mares,
a través de los cielos
unimos las manos
y alto volamos.

En nuestra familia
somos todos hermanos,
y nos enlazamos
desde el mar al monte;
gotitas de lluvia
formamos un río
y sabios fuertes
el profundo mar...

A través de los mares,
a través de los cielos
unimos las manos
y alto volamos.

Pensemos de pie,
de pie con orgullo
celebrar la vida,
tu vida y la mía;
aunque vivimos
tan lejos del otro
te creo mi amigo,
amigo del alma...

A través de los mares,
a través de los cielos
unimos las manos
y alto volamos.