

Sixth Framework Programme

Life Sciences, Genomics and Biotechnology for Health
Specific Targeted Research Programme

Prader-Willi Syndrome: a model linking gene
expression, obesity and mental health

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Outline

- Establishing an EU PWS research network
- The future use of the PWS clinical research database
 - Demonstration of the database (Marion and Joyce)
- Ideas for future collaborations (after coffee)
 - Perspective of PWS Associations
 - Best practice guidance
- Informal discussions (after lunch)

Establishing a network

What have we learnt from the current EU project?

- Added value
 - Basic science
 - Clinical
 - National Associations
- Importance of a clear focus for the project
 - Agreed research
 - Integration of research
 - Advancing understanding
- Establishing and maintaining the identity of the collaboration
 - Mutual respect and trust
 - Yearly event
 - Communication (web-site etc)
 - Outcomes

Establishing a network

Components at a national level

- National groups active in PWS research
 - National studies
 - Particular interests and expertise
- Links at national level between research groups and national PWS Associations
- National infra-structure to support research and the dissemination of findings

Establishing a network

Components at an EU level

- A range of basic science, clinical, and research expertise so that different approaches to particular issues can be used
- Links to EU national PWS Associations to support:
 - Generation of research ideas
 - Recruitment of participants
 - Dissemination of findings
 - Changes in policy and practice

Establishing a research network

Hypotheses

- Collaborations work best when it is to everyone's advantage that they work (Is this too cynical?)
- Meetings, networks and collaborations work best when they have a clear and agreed focus:
 - Supporting people with PWS and their families and exchanging ideas (IPWSO, Cluj Romania)
 - Developing good practice guidance (Toulouse, France)
 - Developing best social care practice (Herne, Germany)
 - Developing the research agenda (Cambridge, UK)

The role of the database in the establishment of such a network

- It is a research tool that makes collaborative research more possible;
- Provides a 'focus' for a research network to relate to 'the network has ownership of it';
- Has tried to model collaborative work through establishing agreed criteria.

Why develop an EU database?

- To enable the reliable and lawful collection, management and analysis of data obtained using agreed methods across many countries;
- Comparisons between countries to enable the influence of different educational, health and social care policies on the lives of people with PWS to be investigated;
- Establishes a critical mass of inter-disciplinary clinical expertise to focus on a rare disorder and the development of best practice across the EU.

Agreed objectives EU database

- To facilitate multi-site, clinical research on PWS
- To standardised assessment procedures so data can be combined between groups and over time
- To reduce the need for different groups to collect the same data
- Accumulated data to allow the testing of novel hypotheses and to enable longitudinal studies
- Cross-cultural and cross-national studies

Support for multi-centred studies

EU Project 6th Framework

Aims

To develop a database that will enable multi-national clinical studies of PWS

Database must be:

- Compatible with EU and national laws
- Accessible from multiple sites
- Support the storage, management, analysis and presentation of cross-sectional and longitudinal data

Use of the database

Database Manual

- Integrity and confidentiality of personal data
 - Consent procedures
 - Anonymous data
 - Long term use of data
- Quality of data stored on the database
 - Quality of data collection
 - Assessments used
- Combining of data
 - Collaborations
 - Anonymous data
 - Publications

Demonstration of the database

The next stage for the database

Final stage of the current EU grant (31st May 2009)

- ‘Test’ the database
- Agree the contents of the database manual
- Agree the framework for the long-term management of the database
- Resolve the following:
 - Ownership of the database
 - Maintenance funding
 - Ethics/consent issues

Long-term support

- At national level
 - Research groups
 - National PWS Associations
- At EU level
 - Rare diseases infra-structure
- At international level
 - ?IPWSO

Possible UK Model

Seek grant funding for:

- Establish database support at UK PWSA
- National database management group chaired by representative from UK PWSA
- Presentation and demonstration of database at PWSA meetings
- Contact of past and present recruits with PWS
 - New consent procedures
 - Up-date of recent clinical information
- Recruit new participants
 - Core clinical information
- Establish long-term recruitment strategy

Tasks

- For research and clinical groups at a national level to consider:
 - Links with national Associations
 - Ethical and legal issues
 - National clinical and research infrastructure
 - Research priorities and national expertise
 - Initial ideas and development of research themes and potential collaborations
 - Developing of protocols – possible funding
 - How can the database help?

Ideas for future collaborations

- Start small
- Iterative process (step by step)
- Use what we have at present
- Develop confidence and through publications etc demonstrate the benefits

General comments

- The importance of establishing and maintaining formal and informal networks within and between countries;
- Understanding the pressures and demands on the different partners
 - PWS Associations (problems of day-to-day life)
 - Clinicians (resources, time etc)
 - Researchers (publications, research assessment exercise, funding)
- Establish a clear understanding of roles and responsibilities of different partners prior to starting a project
- Resolve disagreements at an early stage
- Appreciate that, particularly for complex and rare disorders, collaborations bring benefits but is hard work!

Future collaborative research across the EU

- What research:
 - Is needed
 - Requires a multi-national approach
- What expertise is needed?
 - Clinical
 - Social science
 - Basic science
- What might be done now and what requires longer-term planning?

Future collaborative research across the EU

- Integration of clinical and basic science
- Quantitative and qualitative research
- Funding at national, multi-national and EU level
- The emergence of research themes and 'leaders'

Research at a national level

Example (mental health in PWS)

- UK population-based study identified the association between PWS and affective disorders
 - Deletion/UPD differences
 - Relationship with age
- Study of specific cohorts of people with PWS established
 - Phenomenology of psychiatric illness
 - Relevance of maternal depression
 - Proposed a 'genetic' explanation of findings
 - 'Human genetic studies':
 - Presence of genetic abnormality of maternal origin in people with delPWS who developed a psychotic illness
 - Further studies of the possible functional consequences of genetic abnormality (in PWS and general population)
 - 'Two hit' model leading to psychosis
- Investigation of possible brain mechanisms
 - Animal models (snoRNAs, 5-HT_{2c} receptor)
 - Ligand based brain scanning technology

Research at an EU level

Example (mental health in PWS)

- Confirmation of findings in a larger sample
- Age of onset, presentation, and course of psychiatric illness in people with PWS
- Aetiology, protective and risk factors for psychiatric illness in PWS
- Relationships between different aspects of the psychiatric and 'behavioural' and physical phenotypes
- Treatment approaches – short and long-term risks and benefits
- Other investigative techniques available across the EU

Future Research

Example (mental health in PWS)

- Treatment trials
 - Prevention
 - Acute
- Outcome studies
- Best practice
- Implications outside of PWS

Discussion

- What could we do now?
- What do we need to do in the future?
- What expertise do we have and what do we need?
- Funding
- Co-ordination