Outline

- What is InterRett?
- Data collection
- Data output
- Challenges
- Opportunities

What is InterRett?

- International project to examine clinical features of Rett Syndrome.
- Funded by IRSA - International Rett Syndrome Association (USA parent association).
- Managed by the Australian Rett Syndrome programme.

Aims of InterRett

- Increase the clinical understanding of Rett syndrome
- Provide a large sample of cases for analysis
- Encourage collaboration among researchers around the world
- Provide an innovative and efficient mechanism to:
  - Disseminate research findings
  - Provide clinical support

International Reference Panel

- 52 members representing 19 countries
  - Researchers
  - Clinicians
  - Family members

- Role of Reference Panel
  - Advise on ethical issues, questionnaire items, database data items
  - Advise on issues of access to information collated in database
  - Advocacy

Data Collection

- Data are collected from two sources
  - Families
  - Clinicians
- Participants can submit data using paper questionnaires or online through our website
- Clinicians with bulk data are provided with a custom database

Family Questionnaire

- Section 1 - Demographics
- Section 2 - Mother's health
- Section 3 - Pregnancy
- Section 4 - Perinatal period
- Section 5 - Early development
- Section 6 - Specialist care, mutation testing
- Section 7 - Language and communication
- Section 8 - Medical history
- Section 9 - Hand use
- Section 10 - Current characteristics

Challenges

- Access for non-English speaking families
  - Volunteers
- Follow-up
  - Time zones
  - Language barrier
- Data interpretation
  - Dates
  - Education system

Cases

- Oct 2003 - present
  - 262 family questionnaires returned
    - Clinician data on collected on 181
  - 44 De-identified family data from China and Israel
  - 289 De-identified clinical data from Spain, Israel and other countries
- Total **595** cases

Data processing

- Process:
  - Data cleaned in File Maker pro
  - Data uploaded onto SQL database server
  - Lasso code manipulates data and creates graphs
- All data are de-identified
- Database accessible to anyone through InterRett URL www.ichr.uwa.edu.au/rett/irsa

IRSA

InterRett - IRSA Rett Phenotype Database

Search the Database

To start searching the database, select your first variable from the pull down list. You can then decide if you would like to view that variable on its own, or graph it compared to another variable (bi-variate). Then click on the **"Display the graph"** button to view your search. You can do as many searches as you wish.

Choose a first variable:

Common pathogenic mutation

Would you like to compare this variable with another variable?

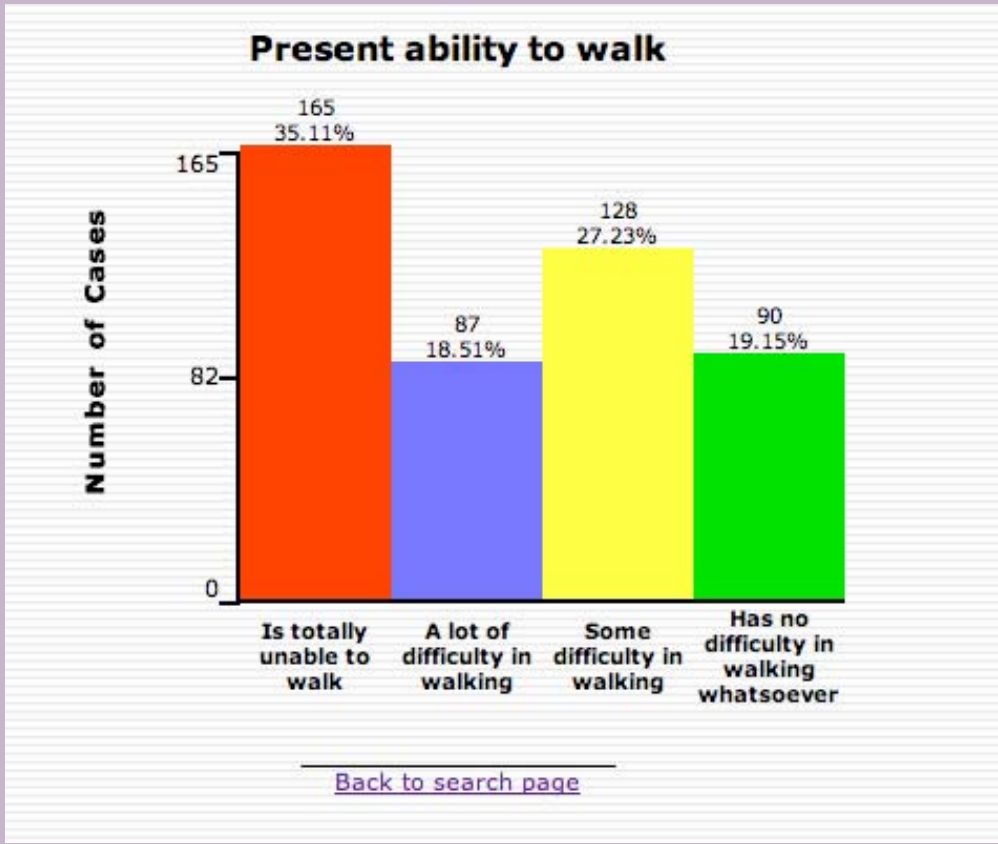
(•) Yes ( ) No

Choose a second variable:

Ever had seizures

- Presence of unusual development or behaviour during first 6 months
- Presence of unusual development or behaviour from 7 to 10 months
- Learned to walk unaided
- Age at first steps unaided
- Clinical diagnosis
- Age at confirmation of diagnosis
- Ever had seizures
- Presence of spinal curvature
- Presence of digestive disorder
- Type of pathogenic mutation
- Domain of pathogenic mutation

Back to main page



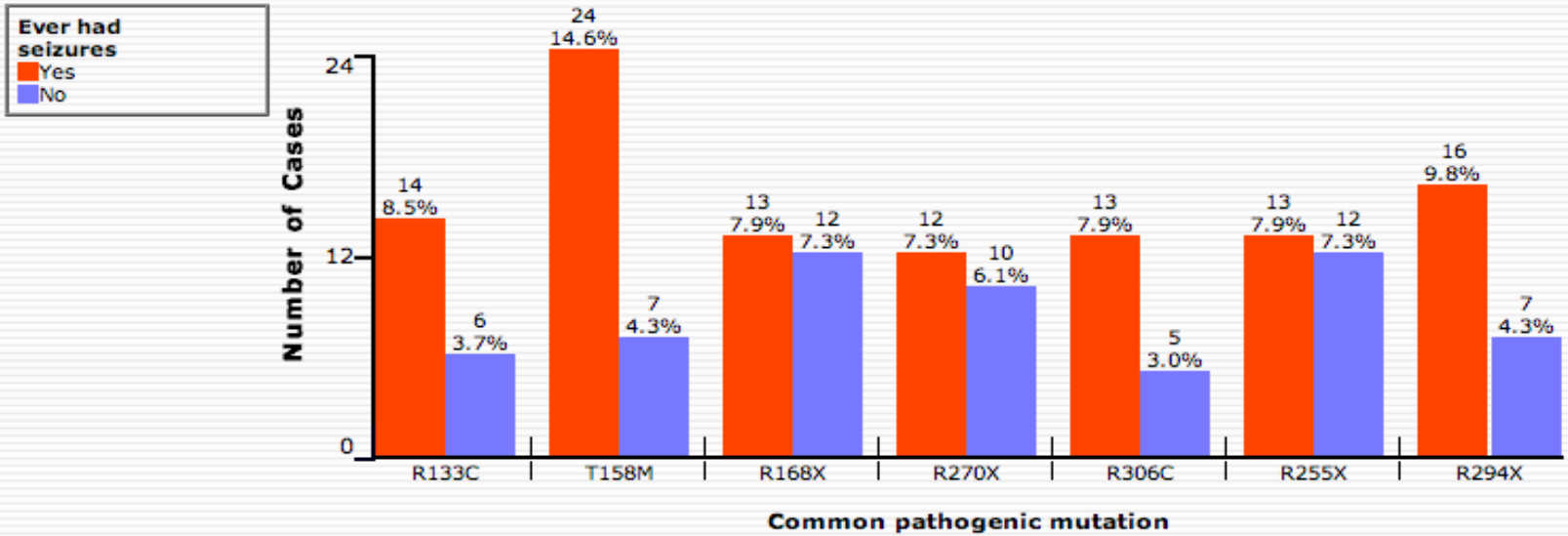
470 cases

90 Can walk

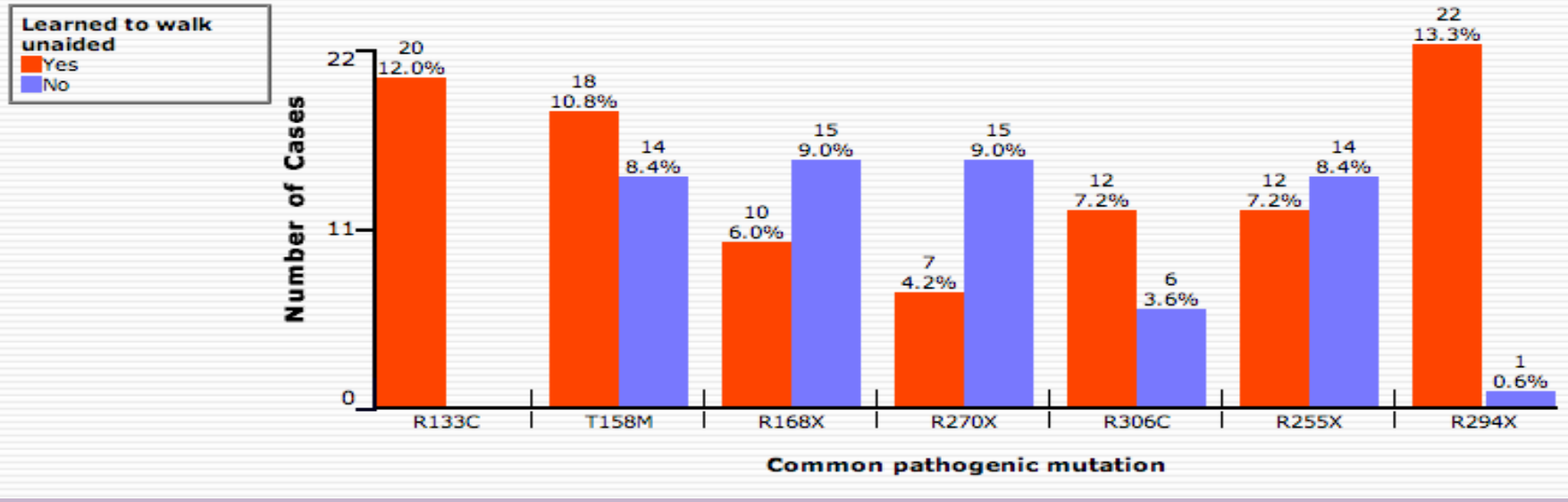
165 Cannot walk

215 Can walk with some level of difficulty

Common pathogenic mutation vs. Ever had seizures



Common pathogenic mutation vs. Learned to walk unaided



Data analysis

InterRett data is included in research studies:

- Lost in Translation: Translational Interference From A Rare But Recurrent Mutation in Exon 1 of Mecp2.

- Genotype and early development in Rett syndrome: The value of international data.
  - Examined whether early development in the first 10 months varied by genotype
  - Statistically significant differences were detected with R255X and R270X having the most severe profile overall.

Data analysis

- Using an international cohort to further investigate the relationship between genotype and phenotype in Rett syndrome.
- X-inactivation study: looking at x-inactivation in specific mutations and using parental samples. The inclusion of InterRett Spanish cases will provide the necessary statistical power that could not have been otherwise obtained.

The future of InterRett

- Invitation to apply for further funding
- Ongoing case ascertainment
- Stage III Output Database
  - More complex searches
  - Searching with limits
- More data analyses
- Building Collaborative networks

Research Challenges

- Gaining support from researchers
  - Issues regarding ownership/authorship
- Lack of standardisation
  - Different protocols administered
  - Variation in severity scales and interpretation
- Lack of infrastructure
  - No central point for raw data, clinical and genetic information, tools and discussion.

Opportunities for InterRett

InterRett is in a unique position to provide infrastructure.

- Current website and database can be developed into a repository of datasets and supporting information.
- Provide a global view of Rett syndrome research data and potential contacts for collaborative work.
- Foster standardisation by providing ‘question banks’ and study guidelines.

Clinical Challenges

- Diagnosis
  - Low awareness
  - Variability
- Knowledge dissemination

Opportunities for InterRett

Clinical support provided:

- Online diagnostic support/training tool.
  - Diagnostic criteria
  - Case examples
- Information on the management of Rett specific problems such as scoliosis and feeding difficulties.
- Information on therapies and support options for parents.

Ester

Ester lives in Hungary. At 3 years of age her development was suboptimal. She was showing signs of regression and developing repetitive hand movements. Her clinicians could not decide on a diagnosis.

Her father searched the Internet and found similarities between Rett syndrome and Ester's behaviour.

The family traveled to her mum's hometown of Belgrade were they obtained genetic testing and confirmed that Ester had a mutation.

Nathan Age 4

- Early development was suboptimal.
- Rolled at 10 months
- Sat unaided at 24 months
- Walked with support at 72 months
- At age 3 the use of single words with meaning was lost.
- He was originally Diagnosed with Angelman Syndrome

Nathan Age 12

With increasing rigidity, spasticity and dystonia there was a major loss of skills at age 10 years including loss of ability to crawl, sit and roll over.

Nathan Age 13 -14

Hand wringing began around 11 years of age and persisted until the age of 14 years when he was no longer able to bring hands to the midline.

General symptoms

- Severe constipation
- Night screaming
- Very cold bluish feet
- Breathholding
- Night laughing

Peg tube feeding was introduced due to oro-motor difficulties at 16 years. A tracheostomy was carried out at 18 for severe obstructive and central apnea.

Nathan Age 18

He was diagnosed with spastic diplegia with significant ataxia and myoclonus before being diagnosed as Atypical Rett at 18 years and 3 months (C1164-1207del44).

Thanks go to...

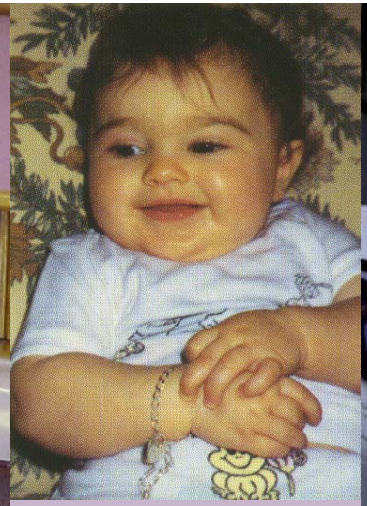
InterRett - IRSA Rett Phenotype Database

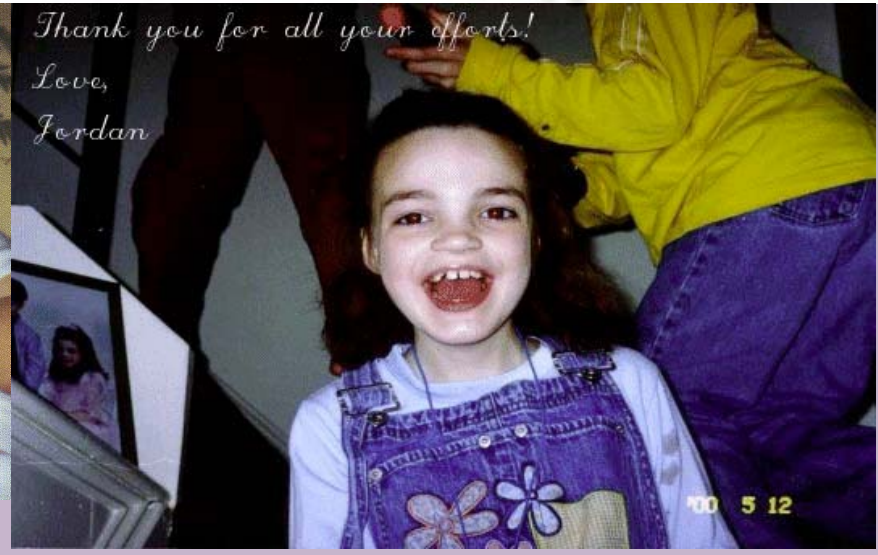
- International Rett Syndrome Association
- The Friends: Institute for Child Health Research
- APSU
- National Institutes of Health
- NHMRC
- The Szili family
- The Olson family
- All the families and clinicians who support the research so well

IRSA

INTERNATIONAL RETT SYNDROME ASSOCIATION

InterRett - IRSA Rett Phenotype Database





InterRett - IRSA Rett Phenotype Database
Telethon Institute for Child Health Research
PO Box 855 West Perth WA AUSTRALIA 6872
Ph: +61 8 9489 7790
Mob/Cell: +61 419 956 946
Email: rett@ichr.uwa.edu.au
URL: www.ichr.uwa.edu.au/rett/irsa