Behavioural phenotype of Rett Syndrome

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Introduction

• What the literature tells us about the behavioural phenotype of Rett Syndrome

• Research purposes
  ✨ Aim
  ✨ Stages

• Where we are now: some findings

• Where next?

• Discussion/Questions
Some findings from the literature

- Behavioural aspects mostly studied are:
  - Autistic features
  - Sleep disturbances
  - Neurological (breathing abnormalities and seizures)
  - Stereotypies
  - Communication and language abilities
  - Genotype-phenotype association
Previous studies

- Mount et al. (2002) behaviours more common in RS
  - hand stereotypies
  - Autistic features
  - Screaming/crying/laughing
  - Fear/anxiety
  - Breathing abnormalities
  - Self-injury

- Coleman (1988) & Samson et al. (1993) reported behaviours other than hand stereotypies, including self-injury, screaming, fear in unfamiliar situations and hyperventilation
Autistic features

- Young et al. (2008) found 17.6% had an initial diagnosis of autism
  - milder phenotype
  - more likely to have some functional use of the hands and to be ambulant
- Percy et al. (1988) compared RS and autism
  - differences in respiration pattern, ataxia, slow movements and hand movements
- Olsson & Rett (1987; 1985) compared RS and autism
  - differences in social behaviour
  - children with RS
    - enjoy social contact
    - made eye contact
    - smiled and looked at people’s faces more
**Communication**

- Eye gaze and looking at another person’s face were the communicative behaviours most often reported.

- Fabio et al. (2009a; 2009b)
  - Non verbal communication skills (i.e. eye-gaze, positive attitude to human face) may facilitate learning.
  - Hand stereotypies could interfere with learning.
    - RS girls responded quickly to presented stimuli when stereotypies were controlled.
Communication

• Strategies to increase communication:
  • Sigafoos et al. (1996) – teaching RS girls the ability to request preferred items
  • Van Acker and Grant (1995) – computerised system to teach RS to make choice
  • Hetzroni et al. (2002) – computer software to teach symbols identification
  • Elefant and Wigram (2005) – requesting a song by eye pointing, nose pointing or touching a symbols
Family studies

- Perry et al. (1992) reported high level of stress, greater social isolation and more health problem.

- Laurvick et al. (2005) factors such as feeding, sleep, behaviour and community participation are most likely to affects maternal mental and physical health.
Research question

• Are specific behaviours associated with Rett Syndrome?
  • autism-like behaviours
  • teeth grinding
  • sleep abnormalities
  • self injury

  or

• Are they simply associated with severe intellectual disabilities in a less specific way?
Research Aims

• Accurate description of behavioural and emotional features of RS

• Behavioural changes across age groups

• Differences in behavioural characteristics among people with RS

• Differences in behavioural characteristics between people with RS and other ID genetic syndromes

• The impact that severity of behavioural and clinical presentation have on family stress and mental health
Stages of the study

- **National survey**
  - Postal questionnaire containing 2 booklets:
    - Behavioural, physical and emotional characteristics of RS family member
    - Family adjustment and needs

- **Behavioural observation**
  - Organization of the behavioural repertoire
  - How environmental conditions might affect behaviour

- **Longitudinal study**
  - Questionnaire repeated after 18 months to address change in behavioural characteristics and family adjustment over time
Measures

- Child/ adult with RS
  - early development
  - current skills
  - RS behavioural characteristics
  - medical problems
  - how sociable
  - mood (& sudden mood changes) and interest in surroundings

- Family
  - stress
  - anxiety and depression
  - positive experiences
  - level of support
  - perception of improvement or deterioration in symptoms
  - experience of siblings
Participants and recruitment

• Letters were sent by the BIRSS to families whose daughter/son had:
  • Classic Rett Syndrome (regardless of MeCP2 mutation)
  • Atypical Rett Syndrome (with MeCP2 mutation)
• 92 families returned completed questionnaires
Where are we now: some findings

• How much do clinical and behavioural problems vary with age?

• How much are family problems related to the severity of clinical and behavioural problems?
Clinical and Behavioural Problems

• Simplified Severity Score
  • assesses 6 features of RS
    • Sitting, Walking, Hand Use, Speech, Epilepsy & Scoliosis
  • On a scale of 0-3 (overall maximum 18)
  • A score less than 9 = mild or less severe

• Rett Syndrome Behavioural Questionnaire
  • Parents rate 45 items in 9 areas
    • General Mood, Breathing Problems, Hand Behaviours, Repetitive Face Movements, Body Rocking and Expressionless Face, Night-time behaviour, Fear/Anxiety, Walking/Standing, Other behaviours
  • On a scale: 0= not true, 1= sometime true, 2= very true in the last 6 months (overall maximum 90)
Family stress and mental health

- Questionnaire on Resources and Stress
  - Includes 16 questions (True/False) on parental and family problems to assess stress

- Hospital Anxiety and Depression Scale
  - Contains 14 items (7 on depression and 7 on anxiety)
    - 0-7 = normal
    - 8-10 = borderline normal
    - 11-21 = abnormally anxious or depressed
Participants

• All participants were female, except 1 male

• Ages ranged from 4 to 47 years
  • Age groups
    • childhood (<12 yrs)
    • adolescence (13-18 yrs)
    • early adulthood (19-25 yrs)
    • adulthood (26+)

• Most lived at home (10% lived elsewhere)

• 74 had Classic RS and 18 had Atypical RS
Diagnosis and mutation in MeCP2
Does severity of phenotype vary with age?

- No systematic trend across age groups
- Only walking and scoliosis varied across the age groups
• Total RSBQ score ranged from 12 to 78 (mean 42)

• No systematic trend across age groups (the higher score in adolescence was not statistically significant)
Are family problems related to severity of phenotype?

• Stress levels varied
  • about half of the families reported low stress
  • the other half reported high stress
• Stress was not associated with
  • age
  • severity score
• Stress was associated with RSBQ score
  • particularly problems in
    • mood,
    • fear and anxiety
    • vacant spells
    • grinding teeth
Anxiety and Depression

- Anxiety and depression levels

![Bar chart showing levels of anxiety and depression](chart.png)
Anxiety and severity of phenotype

• Anxiety was not associated with severity score

• Anxiety was associated with
  • age
    • anxiety was higher in families with a younger child
  • RSBQ score, particularly problems in
    • mood
    • breathing abnormalities
    • face movements
    • fear and anxiety
Depression and severity of phenotype

- Depression was not associated with
  - age
  - severity score

- Depression was associated with RSBQ score
  - particularly problems in
    - mood
    - body rocking
    - fear and anxiety
What does all this tell us?

- There appear to be no significant differences between the four age groups.
- Although families of younger children feel more anxious.
- Limitations:
  - Small numbers in each group.
  - We have looked at the group as a whole and not at individuals cases.
  - Other factors may be associated with age which we have not yet considered.
What does all this tell us?

- Severity of clinical symptoms (the severity score) was not associated with family stress or mental health.

- Increased stress, anxiety and depression were related to the severity of behavioural presentation (as measured by the RSBQ).
  - Breathing abnormalities, changes in mood, repetitive movements and fear and anxiety in the child are linked to increased parental stress, anxiety and depression.
Where next

- Behavioural Observation (ongoing):
  - 10 families with girls with RS and confirmed MeCP2 mutation
  - Video recording of day to day activities in school, home, day centre etc.

- Longitudinal study: we will be sending some further questionnaires (not the full set!) to the families that returned them in the first stage (from March, 2011 onwards).

- Continue to recruit families (if you have not received an invitation letter or have changed your mind, you can still participate!)

- Linking with other universities to
  - compare behavioural characteristics of Rett Syndrome with other rare genetic syndromes
  - refine the behavioural measure for Rett Syndrome
Thanks

• To all the girls and the one boy

• To all the families that have agreed to give some of their time to fill in the questionnaires and allowed me to video record their daily life

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References


