



The Australian **Rett Syndrome Study**

Report 2006



The Australian Rett Syndrome Study

Telethon Institute for Child Health Research
100 Roberts Road, Subiaco
Western Australia 6008

t 61 8 9489 7790

f 61 8 9489 7700

e rett@ichr.uwa.edu.au

w www.ichr.uwa.edu.au/rett/aussierett

Edited by Paula Dyke
Dr Helen Leonard

Production and graphics by Heather Monteiro and Carol Philippe

Suggested citation:

Dyke, P., Leonard, H. (2006) The Australian Rett Syndrome Study Report 2006.

Telethon Institute for Child Health Research, Western Australia.

Contents page

Foreword	2
Introduction	4
The Australian Rett Syndrome Study	4
What is Rett syndrome?	5
How is Rett syndrome diagnosed?	6
Rett syndrome in Australia	7
About this report	8
Part 1: ‘Families’ descriptions of Rett syndrome and their experiences of living with a daughter with this condition’	9
About the families who completed the questionnaire	10
Diagnosis of Rett syndrome	15
Characteristics of Rett syndrome	19
Medical services	27
Educational, community & therapy services.....	35
Evaluation of therapy services	41
Common areas of concern for families.....	51
Part 2: ‘Current research and publications’	61
Genetics	62
Scoliosis research	66
Densitometry study	67
Epilepsy study	68
The video study	69
Publications	72
Presentations.....	74
Study personnel, students and collaborators in 2006	76
Acknowledgements	77

Foreword

by Dr Helen Leonard

It is with great pleasure that we publish this second report of the Australian Rett Syndrome Study, now known affectionately as AussieRett.

The principal purpose of this report is to provide feedback to families and others involved with Rett syndrome in Australia about the information we are collecting as well as updating them on our recent research publications.

Much has happened in the four years since our original report. Of particular significance was the awarding of funding by the US National Institutes of Health and the Australian National Health and Medical Research Council to support continuation of our research activities from 2004 through to 2008. As a result of this we have been working very hard over the past few years to demonstrate to these funders the value and worth of investing in our Australian research. We do this by producing scientific publications which are then available to researchers and practitioners working with children and adults with Rett syndrome. These publications, listed for you in the report, are contributing to the global body of knowledge about Rett syndrome. We feel particularly privileged to be able to use the data provided by Australian families for this purpose.

Once again we would like to express our sincere appreciation to all the families who have contributed to and continued to support this study, some for as long as 13 years. We also thank the many Australian clinicians who have also been involved. Moreover we acknowledge the roles of the Rett Syndrome Association of Australia, the Rett Syndrome Australian Research Fund and the Australian Paediatric Surveillance Unit. As well as providing an update on our research we have decided to focus this time on areas which we hope will be of particular relevance to families. We hope that the report will be of interest and value to all its readers.

Regards



Dr Helen Leonard
The Australian Rett Syndrome Study
Telethon Institute for Child Health Research

by Mr Bill Callaghan

Since its inception in 1993, the Australian Rett Syndrome Study, has gone from strength to strength, particularly in terms of projects undertaken, publication of findings, awareness raising, collaboration with other Australian and overseas researchers, and its relationship with Rett syndrome families.

Those families are to be commended for their ongoing participation and it's gratifying to see the information that they have provided to the Study, being utilised to produce this Report. What makes this publication extra special is the data concerning their experiences in such areas as education and health services, topics which to date, have rarely been examined in the literature available on Rett syndrome.

In tandem with the other information that this Report provides, knowledge of the syndrome and its impact on the family has been greatly enhanced as a result.

Regards,

Bill Callaghan
President
Rett Syndrome Association of Australia

Introduction

The Australian Rett Syndrome Study

The Australian Rett Syndrome Study is based at the Telethon Institute for Child Health Research located in Perth, Western Australia.

The Institute has a national and international reputation for conducting pioneering and important research into many aspects of child health research, including birth defects, infectious diseases, cancer, asthma and childhood disabilities.



The Australian Rett Syndrome Study was established in 1993, and operates in collaboration with a number of hospitals and universities in Perth and around Australia. The central focus of the study is to collect data about Rett syndrome in Australia so that parents can be provided with current and accurate information about the progression of the disorder, the variability in its severity and the best ways of managing the care of children and women with Rett syndrome.

A unique feature of the study is that it involves almost all families in Australia who have a daughter with Rett syndrome born since 1976. This makes the study 'population based' allowing the researchers to be confident that their findings will be applicable to the majority of girls and young women with Rett syndrome.



What is Rett syndrome?

Rett syndrome is a relatively rare but serious neurological disorder, most commonly seen in females and very rarely in males. It was first described by the Austrian neurologist Andreas Rett, however it did not become internationally known until a paper on the disorder was published in 1983 by Dr Bengt Hagberg and colleagues¹.

In general, the child with Rett syndrome shows an early period of apparent normal or near normal behaviour, although recent research is indicating that very subtle neurological signs may be evident in the early months of life².

This period is followed by what appears to be the cessation of developmental progress, beginning most commonly between 6 – 18 months of age and characterised primarily by a loss of communication skills and the development of unusual hand movements or stereotypies. Usually at this time the child may also appear to be particularly distressed and agitated. Following this period of regression, girls tend to become happier and once again may be able to learn new skills, reaching relative stability in their condition in the middle to late adolescent years.

Rett syndrome is usually associated with significant physical and intellectual disabilities, although there is great variation among outcomes for girls with this condition. While some girls and young women maintain good general health, many develop epileptic fits or seizures, abnormal breathing patterns, gastrointestinal problems, muscle contractures and spinal curvature or scoliosis.



How is Rett syndrome diagnosed?

Until recently, Rett syndrome was only able to be diagnosed clinically when a number of certain physical and behavioural features were present (some of these include poor head growth, slow general development, repetitive hand movements, and dyspraxia). Girls in whom all the features are present are considered to have 'classical' Rett syndrome and girls with most, but not all, of the features are thought to have what is known as 'atypical' Rett syndrome. Because of the often unclear and confusing nature of the clinical presentation, many families had, and still may have, their children misdiagnosed as having cerebral palsy, autism or some type of non-specific developmental delay.

Since 1999, a genetic breakthrough by Dr Huda Zoghbi in Texas in the United States of America has now allowed Rett syndrome, in the majority of cases, to be confirmed by a simple blood test. This disorder has been found to be associated with an abnormality in the *MECP2* gene which is located on the X chromosome. This gene is thought to play an essential role in development in the early years of life, as at certain times during development some genes need to be switched on and at other times switched off. The *MECP2* protein is involved in switching off other genes and an abnormality in this protein may result in it failing to regulate the activity of specific genes at key times in development. It appears to affect primarily the brain and neurological system, explaining many of clinical features seen in girls and young women with Rett syndrome.

Since the discovery of the association between abnormalities in the *MECP2* gene and Rett syndrome, researchers have been able to investigate whether there is a relationship between specific mutations and the severity of clinical features in Rett syndrome. Understanding the link between the gene mutation and the presentation of Rett syndrome will give parents and health professionals a better 'prediction' about development and the potential health conditions which may occur in an individual child. This information will be of use both for families at the time of diagnosis and in the planning of the long-term management of their daughters. Dr Helen Leonard, working with researchers from Perth, other parts of Australia and around the world is heavily involved in this aspect of the research, using data obtained from Australian families.



Rett syndrome in Australia

One of the key aims of the Australian Rett Syndrome Study is to answer the question 'How common is Rett syndrome in Australia?' This information is very important to ensure that the planning for the provision of services for these children and adults can be made as accurately as possible. By the end of 2004, 278 cases of Rett syndrome had been identified in Australia in individuals born since 1976. Approximately two thirds of these cases fit the clinical picture of 'classical' Rett syndrome.

Most (244) of those clinically diagnosed with Rett syndrome in this group of cases have undergone genetic testing, with 73% being found to have an abnormality in the *MECP2* gene. By the end of 2004, 25 of these girls and young women were known to have died, most commonly from respiratory problems such as pneumonia. The map of Australia below shows the distribution of Rett syndrome cases by State in 2004*. In this country, it is estimated that about 1: 8,500 girls or approximately 15 girls per birth year will be diagnosed with Rett syndrome by the age of 15 years.

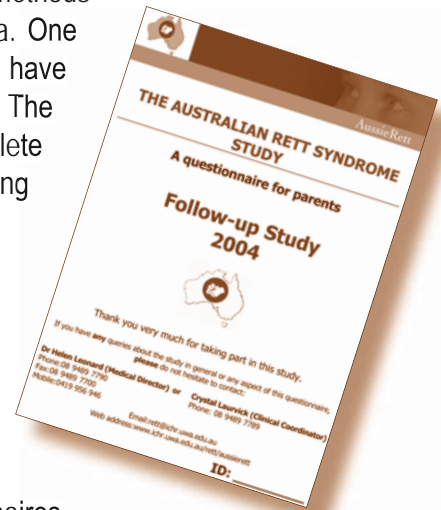


* Excludes the 25 females who are known to have died, and the two boys who are part of this population

About this report

The Australian Rett Syndrome Study uses a variety of different methods to gather data and information about the syndrome in Australia. One of the most important methods used is to survey families who have daughters with Rett syndrome approximately every two years. The survey consists of a detailed questionnaire that families complete over the internet or return via mail, the first questionnaire being completed by families in the mid-late 2000 period.

In 2004/2005 families completed a third questionnaire with each questionnaire focusing on gathering important information from families in relation to a range of functional and behavioural abilities, medical and therapy services, and schooling and daytime activities.



The information provided by families as a result of these questionnaires has been vital in undertaking a number of important pieces of research. For example, studies related to epilepsy, scoliosis and effects on the health of families have all been published in internationally distributed journals and helped the international research and health professional community in 'fitting together the pieces' of Rett syndrome. However, this present report has been essentially written for families. The content has been taken directly from the answers given by families and carers to the most recent questionnaire, and in this way aims to focus on 'Families' descriptions of Rett syndrome and their experiences of living with a daughter with this condition'.

While it is hoped families will find the report of value, it is anticipated the information will also be useful to health professionals and clinicians working with girls and young women with Rett syndrome. In addition, some of the information provided in this report reflecting families' impressions of services is also of importance to policy makers and organisations involved in the planning and provision of services to families with daughters with Rett syndrome.

References

- ¹ Hagberg B., J. Aicardi et al. (1983). A progressive syndrome of autism, dementia, ataxia, and loss of purposeful hand use in girls: Rett's syndrome: report of 35 cases. *Annals of Neurology* 14(4):471-9.
- ² Einspieler C., A. Kerr et al. (2005). Abnormal general movements in girls with Rett disorder: the first four months of life. *Brain & Development* 27:S8-S13.
- ³ Amir R.E., I. Van den Veyver et al. (1999). Rett syndrome is caused by mutations in X-linked *MECP2*, encoding methyl-CpG-binding protein 2. *Nature Genetics* 23(2):185-8.



PART 1

'Families' descriptions of Rett syndrome and their experiences of living with a daughter with this condition'



About the families who completed the questionnaire

A total of 202 questionnaires were completed in 2004/2005, 171 by families and 31 by carers of young women living in residential care. Throughout this report, for brevity, families and carers will be referred to as 'families'. Also while it is known there is a very small number of boys in this particular population the report will only use 'daughters' or girls and young women when referring to the person with Rett syndrome.

In the questionnaire families were given the opportunity to make comments within the different sections, many of these comments have been used as 'direct quotes' in this report. To help ensure anonymity where a daughter's name or initial was used in the quote this has been replaced by 'my/our daughter'.

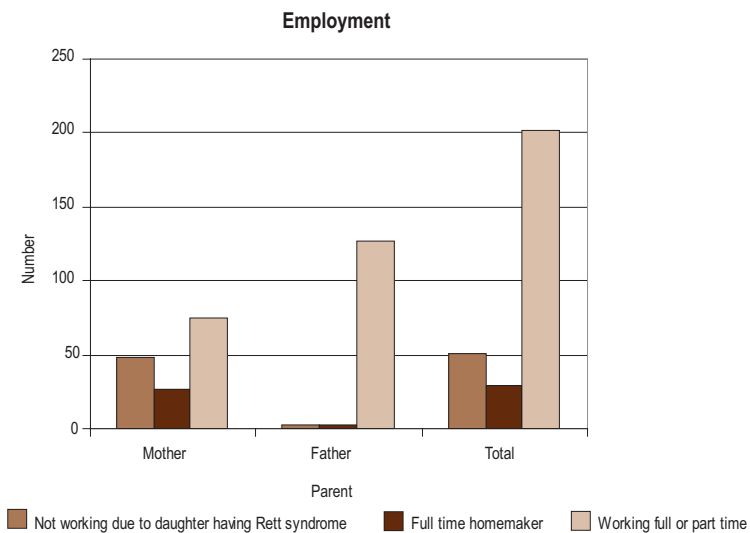
One hundred and fifty nine families indicated that their daughter lived at home. Fifteen families reported their only child was their daughter with Rett syndrome. One hundred and fifty families indicated that they had other children other than their daughter with Rett syndrome, with some families caring for more than one child with a serious disability or medical condition. The average age of the girls and young women with Rett syndrome at the time the questionnaire was completed was 15 years, with the youngest child being 2 years old and the oldest woman 29 years.



Employment

Families indicated their current day occupations and employment, and where appropriate, mothers and fathers were asked to answer this question separately.

Almost one third of mothers who answered this question indicated that they were not working due to their daughter having Rett syndrome, although nearly half of mothers were working either full or part time. Three fathers indicated they were not working due to their daughter having Rett syndrome.



Mothers and fathers were asked if they would be in the same employment situation if they did not have a child with Rett syndrome. While most of the fathers indicated their employment situation was unlikely to be much different, some fathers stated they had given up opportunities for career advancement and higher managerial positions due to the additional stress it would create on the family; not accepted or taken up preferred choices of country positions or overseas postings due to lack of services for their daughter; and were more conservative and risk averse in their career choice.

Some of the answers given by or about fathers to this question are indicated below:

'M was originally employed by a bank ...he took redundancy because we would not move around the State, which meant no promotions because of our daughter with RS'

'I'm an IT professional...possibly would be working or would have work in Europe and North America...have had lots of offers to work abroad but could not due to my daughter having Retts'

'Possibly...however since our daughter's diagnosis he has become more risk averse and conservative in his outlook'

Most women who indicated they were full time homemakers were happy with that choice. On the other hand many of the women who were in current employment indicated they would be working longer hours if they didn't have a daughter with a disability. Some mothers stated they would be working in a preferred area of career choice rather than a current position that they didn't particularly enjoy but that allowed them the flexibility to care for their child. The majority of women who indicated they were not working due to their child having Rett syndrome reported their preference would be to be in the workforce.

Some of the answers given by mothers to this question are indicated below:

'Had high level secretarial government job prior to my daughter....unable to work hours or cope with added stress levels or keep all appointments necessary for her'

'I work at TAFE because I can do half days and night time work....I would go back to High School work but I've lost skills...because I left work because of my Rett daughter....hard for me to update skills when I'm caring for my daughter'

'I am a medical scientist previously having worked for private pathology labs or in large public hospitals...not able to do this work now because of the hours required....lack of out of home care for her if I worked nights or weekends'

'Never had the opportunity to work since having children....Rett syndrome dominates your whole life'

Health insurance and transport

Over 90% of families indicated that their daughter with Rett syndrome had a health care card, with just under half of families also having private health insurance for their daughter. Very few families indicated they had taken out private health insurance because their child had Rett syndrome.

Families were asked whether they thought their current transport is reliable and adequate for their family. Just over half of families said their transport was almost always dependable, with 27% stating it was usually reliable. About 20 families reported that transport for their family was consistently unreliable.

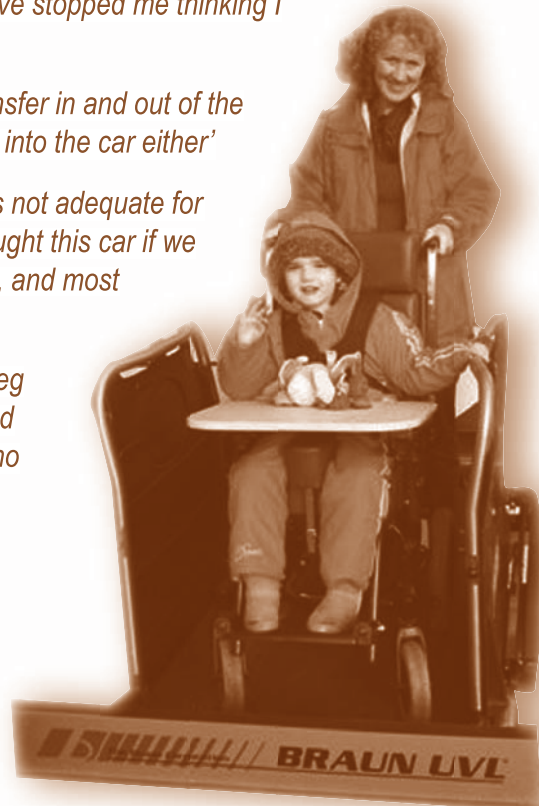
Several families commented on the fact that while they might have dependable transport, it was often inappropriate now that their daughter with Rett syndrome was growing and getting older. Many families stated their need to purchase a van or similar alternative to allow for their daughter to be transported safely, as they were becoming too heavy and awkward to lift into the family vehicle. Most State government equipment schemes in Australia cover the costs of wheelchairs, hoists, etc to allow for safe transport of a person with a disability. However it is entirely up to the family to purchase the large van required, at a cost that is not feasible for many families.

'Car is adequate for all family members except Rett daughter...though of course we manage. A wheelchair accessible vehicle would have been one of those things that would have made a HUGE difference to how we spent our leisure times as whole family...how we accessed the community...not to have to lift wheelchairs in and out of the boot for the last 10 years would have stopped me thinking I didn't want to go out'

'Our daughter is getting very heavy for me to transfer in and out of the car on my own...the wheelchair is not light to lift into the car either'

'We recently purchased a 4WD as our sedan was not adequate for our daughter's needs....we would never have bought this car if we didn't need to...it is easier to lift her in and out of , and most importantly a lot more comfortable for her'

'We can only fit usually one piece of equipment (eg pram or walking frame) in the car at one time and it takes careful arranging to do that....definitely no room for passengers'



Family Income

Families were asked to estimate their gross combined parental income (not including benefits and pensions) for the financial year of 2003/2004. One hundred and thirty two families answered this question, with only 38% reporting a combined income of \$52,000 or more. Thirty per cent of families indicated that their income was somewhere between \$20,000 and \$42,000, and 22% stated their combined income was less than \$21,000 per year. Families were also asked to choose a phrase that best described their money situation; the percentage of families' replies to each statement is shown below.

- We can save a bit every now and then: 42%
- We have just enough money to get us through to the next pay day: 33%
- We are spending more money than we get: 14%
- There's some money left over each week but we just spend it: 7%
- We can save a lot: 4%

Families with daughters with Rett syndrome clearly incur significant financial compromise in providing the best care and a secure environment for their children. Many families indicated the considerable adaptations in their work and employment opportunities that they have had to make to ensure they have the flexibility to adequately care for their daughters' needs. It is significant to note the influence of the impact on the families' financial but also physical and emotional resources as their child grows into an adolescent and woman. For example many highlighted the difficulties in being able to afford suitable transport for their daughter. It is important that policy makers are aware of the increasing needs of the disability population as they move into adulthood. These needs may often be related to transport and this has important ramifications for families and their daughters with Rett syndrome in terms of their access to the community and general quality of life.

Despite the difficulties faced by families with a daughter with Rett syndrome, it is clear that for most families all of their compromises are a 'labour of love' that is best summed up in the comments from one mother:

'I would like to think I would have followed a career path of some kind...now, with current changes in living arrangements for my daughter hopefully I can decide what I want to be when I grow up...I am happy and love life so without my daughter with Rett syndrome maybe I wouldn't be who I am today'

Diagnosis of Rett syndrome

Families indicated that the most common age at which their daughter was diagnosed with Rett syndrome was three years of age, and the average age four and a half years. Of the families who completed the questionnaire, the youngest age at which a child was diagnosed was 10 months and the oldest was 16 years.

The diagnosis

Families were asked to indicate what difference a diagnosis of Rett syndrome had made to their family and the types of services and care that are available to their daughter. The majority of families reported that having a diagnosis had made a difference: primarily in the areas of 'knowing what to expect for the future'; 'paperwork and bureaucracy'; in dealing with health professionals; and in linking with other parents and support networks.

'The day to day management of our daughter is unchanged due to having a diagnosis.....the diagnosis however gives us an idea of our daughters future/her prognosis.....this has been taken into account when making decisions about such things as surgery for scoliosis'

'It has stopped us exploring numerous alternative therapies and 'cures'....after the initial shock of diagnosis, we are calmer within ourselves and with time has come acceptance.....having a diagnosis has made it easier to deal with government agencies'

'A diagnosis has been a valuable source of information to be able to talk to other parents for advice on all aspects.....just to have an idea of what might happen now and in the future'

'Service and care has not changed due to late diagnosis...it has made a big difference to us as we feel many questions have now been answered...it all suddenly makes sense.'

A small number of families made comment that having a diagnosis of Rett syndrome had made 'little difference' and that it had not changed services as they received 'none' or 'very little':

'Most people haven't heard of Rett syndrome and we usually have to do an awful lot of explaining ...at times makes it very difficult for the whole family unit'

'Now that she is an adult NONE...she has lost all the support she had as a child'

'It has made me stay in a State away from my family so I am close to all services for my daughter'

'The diagnosis simply helped us to know what it was not, and what the future would hold. I don't know that we particularly benefited from particular services ...they were not available when she was younger when we needed them more'



Diagnosis before the onset of symptoms

Families were asked if they would have preferred an earlier diagnosis, such as a diagnosis before the onset of symptoms. Of the 155 families who answered this question, 61% said they would have preferred an earlier diagnosis, 21% of families said they would not have liked this to occur with 17% of families being unsure. Some of the comments from families who would have preferred an earlier diagnosis were:

'Yes, because doctors then, 20 years ago, said it was all in the mind of the mother... there was nothing wrong'

'It would have been wonderful...saved us from total feelings of helplessness as we watch our daughter go from a normal little girl to losing her abilities to do things and just going backwards...and doctors thinking her parents were nuts and not able to answer our questions'

'Yes, it may have helped me to understand why my daughter never made progress regardless of how much time I spent on her Early Intervention program. I would have felt less guilt about not doing enough.....I was constantly chasing answers and trying to do more'

'Yes, it hit me like a bomb....to be told that there is something wrong with your daughter at birth would be devastating...but to have one that is so normal and then be told she will lose all her skills including communication is something I wasn't prepared for...we could have videoed more of her precious moments...like saying her first words'

'Yes, we would not have had to put our daughter through numerous blood tests and other tests....It would have saved us a lot of money for numerous test trips, time taken off work and would have prepared us for her regression instead of living a nightmare not knowing what had happened to our little girl'

'The earlier the diagnosis the better prepared the family can be...although I'm not sure anyone would believe where the road is going to take you...maybe therapies and support could be planned or even put into place proactively, rather than reactively or not at all in the present case'



For those families who did not want a diagnosis before symptoms appeared or were unsure, one of the important considerations was whether it would have made any difference to the progress or treatment of the condition. Some of the comments from these families were:

'Our daughter was diagnosed at three by Drs. ...by test when she was 9...not sure it would have made much difference clinically but emotionally it would have been harder, waiting and watching for changes'

'No, I probably wouldn't have believed it...However, once symptoms are present you are desperate to know the reasons why'

'Only if something could be done to reduce the severity of the symptoms or make a difference to her life...otherwise my enjoyment of her as a young baby would have been clouded by what I was waiting for in the future'

'No...we enjoyed the first 8 months of our daughter's life not expecting there was a problem...after that our world came tumbling down around us...we would not have wanted to be robbed of those first 8 months'

'Unsure, if it had made a difference to the progression of the condition'

Genetic testing

Families were asked if it would have been helpful to have had a genetic test available at the time their daughter was diagnosed, and 117 (79% of those who answered the question) families reported that they would have liked such a test. Fifty four families didn't answer this question with half of these families having daughters who are now young women. This is most likely to have been due to some of these women living in residential care, and the questionnaire being filled out by a carer not a parent. Families with daughters aged between 8 and 13 years were more likely to indicate they would have liked to have had a genetic test at the time of diagnosis (81%) than families with younger or older girls.

Genetic testing for abnormalities of the *MECP2* gene is currently undertaken either through the Western Sydney Genetics Program at the Children's Hospital, Westmead or through the Neurogenetics Department at the Royal Perth Hospital. The basic testing will identify the majority of those abnormalities which can be detected. A further small percentage can be found using specialised testing known as multiplex ligation-dependent probe amplification (MLPA) analysis. The time taken to provide a result can vary from one to six months and negative results may take longer than positive results. Screening for the rare exon 1 mutations is available in selected cases at the Westmead laboratory, and screening for *CDKL5* (the second Rett gene) is only carried out on a research basis at Westmead.

A diagnosis of Rett syndrome for all families brings emotions of shock, devastation and profound grief before, often after many years, there is a sense of 'acceptance' of their daughters disability. However, the often misdiagnosis of Rett syndrome as other serious developmental disorders (eg cerebral palsy, autism) causes confusion and adds additional stress to families who are already under significant duress. The increasing use of genetic testing will, it is hoped, reduce the occurrence of misdiagnosis and allow for earlier accurate diagnosis of Rett syndrome.

Families in this study commented that for most, the diagnosis of Rett syndrome has allowed them to:

- Deal with bureaucracies more efficiently.
- Assist them with knowing what the future may hold and their planning for the future.
- Help them to work more effectively with health professionals in the care of their daughter.
- Receive support and information from other parents with girls and young women with Rett syndrome.

'When she was diagnosed it was quite full on with Drs appointments and therapy sessions...now though we just live each day as it comes and our daughter is the core of everything we do. Her happiness is paramount and we are no longer consumed with trying to gain therapy services for her....we don't need to 'fix' her...we think she is pretty perfect as she is'.



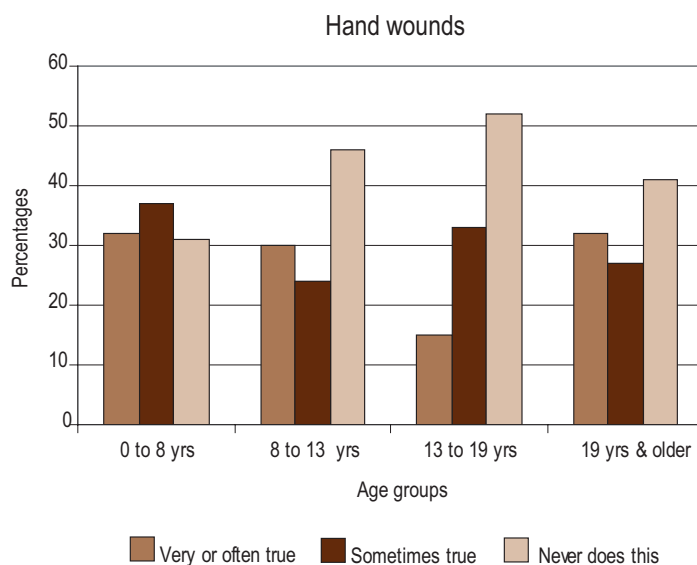
Characteristics of Rett syndrome

Several sections of the questionnaire asked families and carers to describe how much their daughter is affected by the various commonly reported symptoms and behaviours which occur in Rett syndrome. This part of the report describes families' responses to a number of questions regarding their impressions of these characteristics.

Stereotypic hand movements

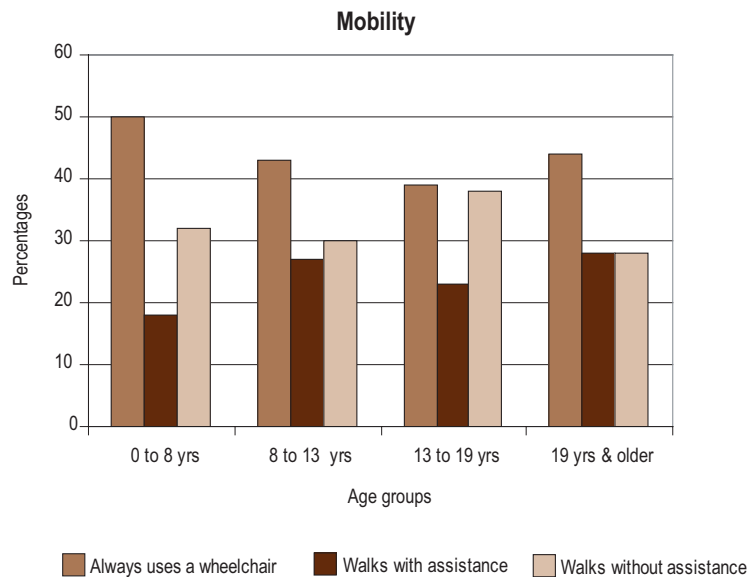
Almost all of the families reported that their daughter displayed stereotypic hand movements, such as wringing, twisting or hand washing, with 87% commenting that these movements occurred almost constantly on a daily basis. The hand movements for most (90%) of the children and adults with Rett syndrome involved both hands, with two thirds of families reporting one hand is generally more active than the other. Hand wringing was the most commonly reported type of hand movement, however families indicated that the girls and young women had a diverse range of movements including twisting, clapping, tapping, hand biting and flicking.

Families often comment that their daughter has wounds on her hands as a result of repetitive hand movements. It appears that girls under eight years of age more commonly have wounds on their hands from stereotypic hand movements, with adolescents least likely to have this particular problem.



Mobility

About half of the children and adults were reported as being able to walk either with or without assistance, and the remainder always used a wheelchair. This did not seem to vary much by age. There were similar proportions in the younger age groups and older age groups retaining some ability to walk or needing to always use a wheelchair, although the adolescent group generally was reportedly the most mobile.

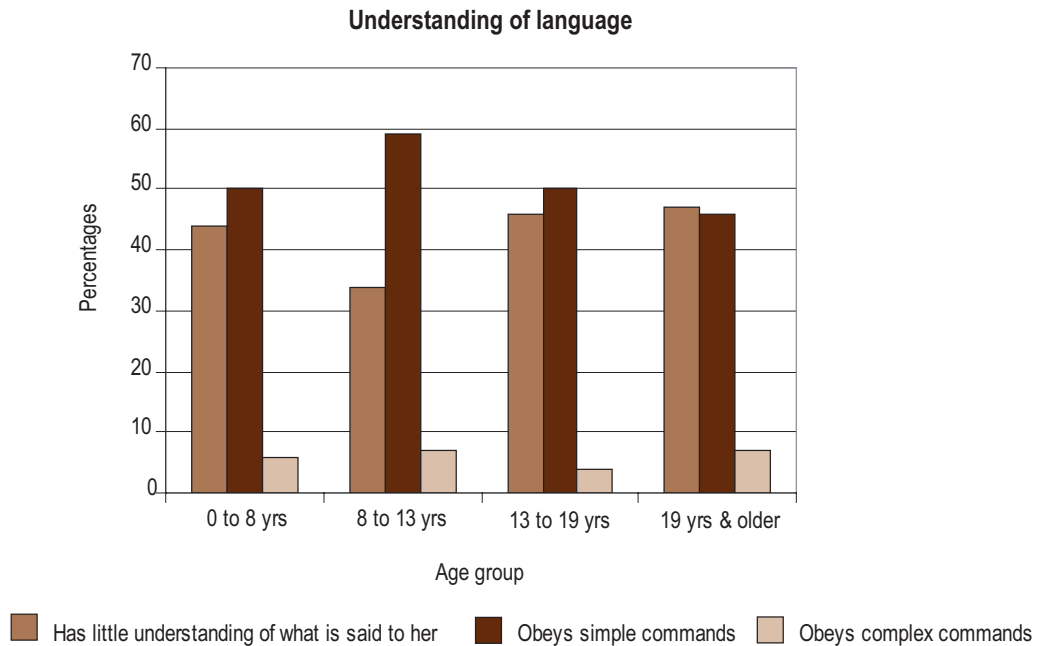


A fairly recent research finding for girls and women with Rett syndrome is that they find it difficult to perform transitional movements i.e. move from one position to another such as lying down to sitting or sitting to standing. This appears to occur regardless of whether they retain the ability to walk or not¹. Families were asked whether they thought their daughter seems frightened when there are changes in her body position, and over a third of families stated they thought this occurred very often. This seemed to be most frequent in girls aged 8 to 13 years (46% of families said this occurred very often) and become slightly less of a problem in young women with Rett syndrome with 35% of families of the older age group reporting fear of movement from position to position as never happening.

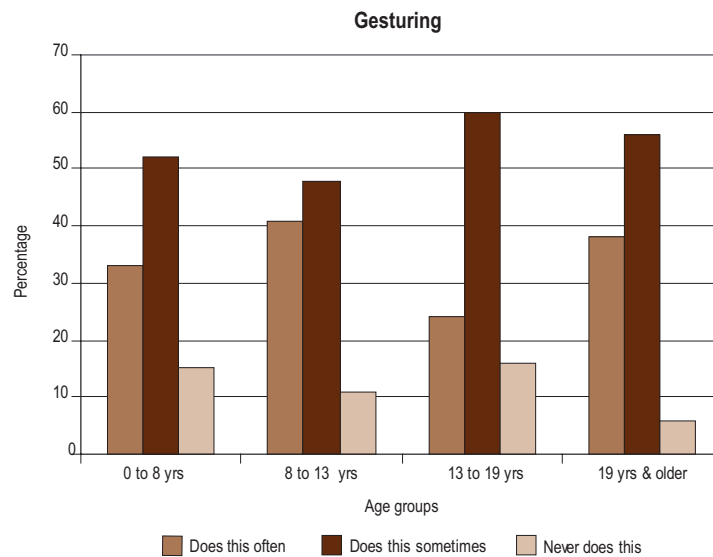
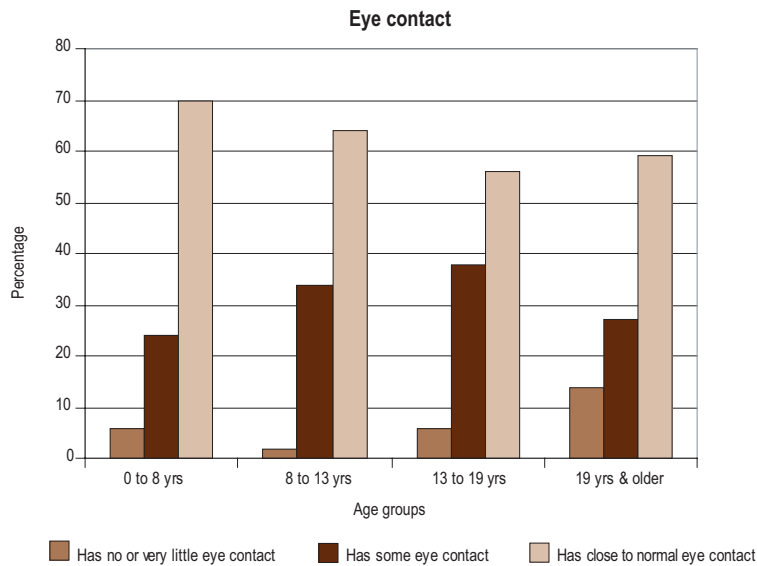


Communication skills

All of the families reported that their daughter had very limited ability to communicate using speech or vocalisation. However, families indicated their daughters had more ability to understand spoken language when compared with their ability to speak or generally communicate.



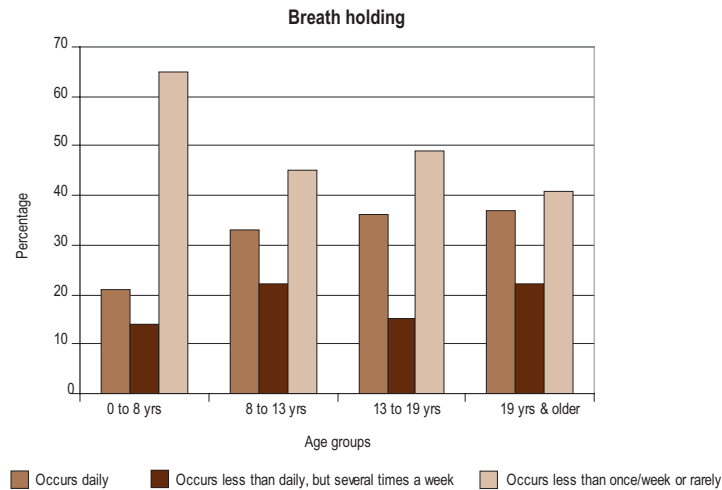
Families also reported that their daughters frequently use eye contact to convey their feelings or simple gestures to obtain attention. Almost 60% of families thought their daughters have 'close to normal eye contact' and over a third of the girls or young women will very often use some sort of gesturing to get a person's attention.



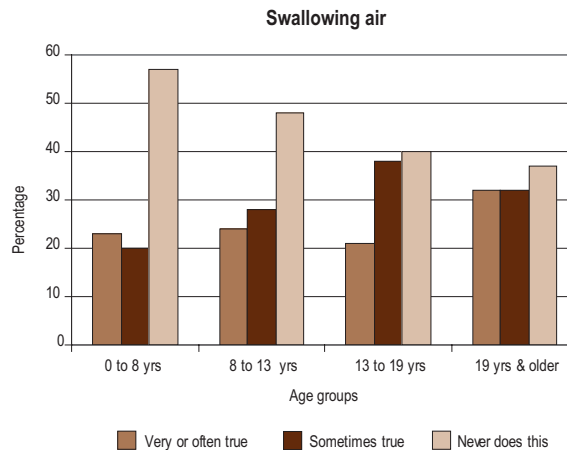
Breathing behaviours

Although hyperventilation and breath holding are known to occur commonly in Rett syndrome, frequent hyperventilation on a daily basis was only reported by about a quarter of families. Sixty per cent of the girls and women were described as hyperventilating less than once a week or rarely. There appeared to be little variation in age groups with regard to how often hyperventilation occurs, with the exception of it being more frequently reported as occurring on a daily basis in girls aged 8 to 13 years.

'Breath holding' was reported by families to occur slightly more frequently than hyperventilation. Thirty two per cent of girls and young women were said to hold their breath fairly constantly on a daily basis and this occurred much less in girls younger than 8 years than in the older age groups.

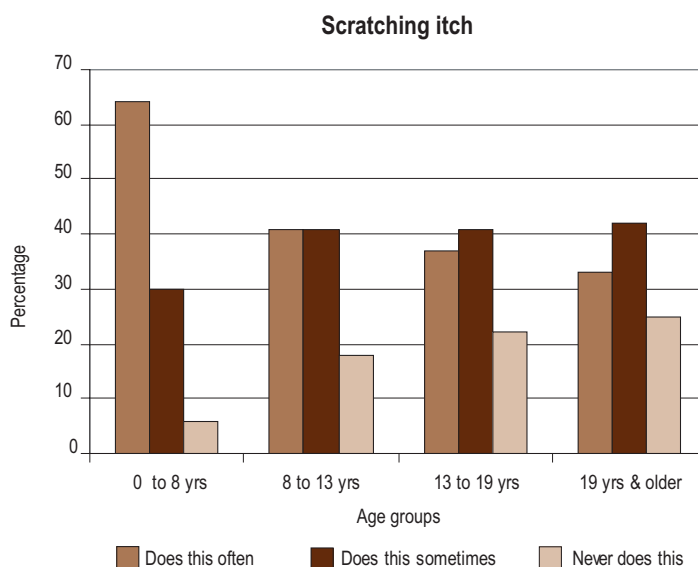


Swallowing air is also another commonly reported behaviour in Rett syndrome. Forty four per cent of families said that their daughter almost never swallows air, although the frequency of this occurring 'often' increased in the older age groups, being most commonly reported in young women with Rett syndrome.

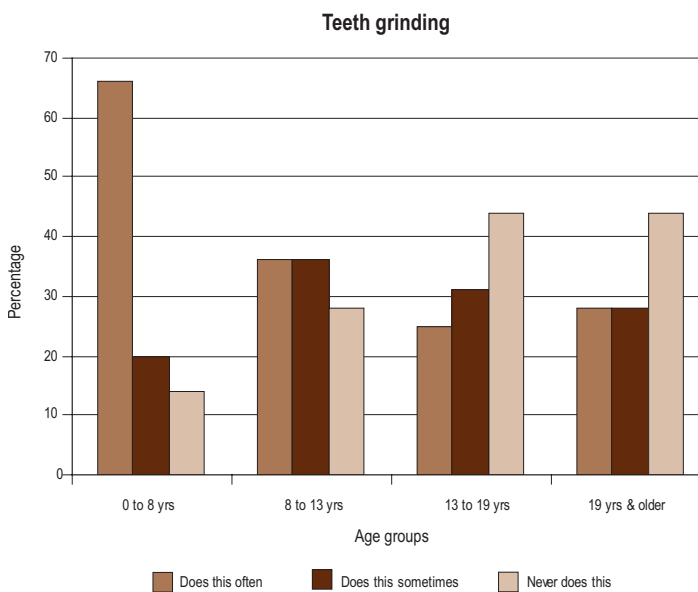


Other reported characteristics

Scratching and itching were fairly common behaviours reported by 42% of families, and this was particularly so in those with daughters under 8 years.

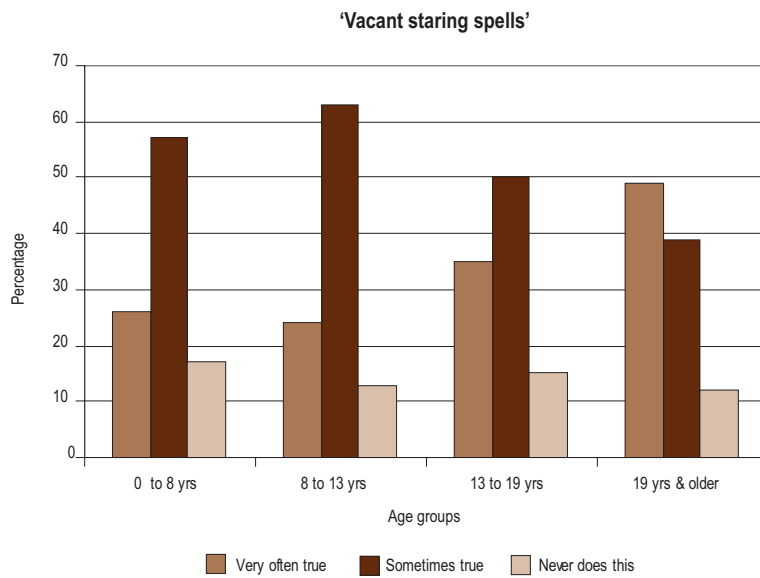


Teeth grinding is another feature commonly associated with Rett syndrome. Two thirds of families answering this question indicated that their daughter ground her teeth more than once a week, and this behaviour was reported much more frequently in girls under 8 years of age.



Families were asked if they thought their daughters appeared miserable for no apparent reason. Over a third of families reported that this was very often true in their girls and young women and only 12 % said that this never occurred. There was very little variation reported across the different age groups.

'Vacant staring spells' are also known to occur in Rett syndrome and were reported by 86% of families, occurring much more often in young women than in children.



Families completing this questionnaire described some interesting variations in behavioural characteristics that they regularly observe in their daughters with Rett syndrome.

- Almost all families described their daughters as displaying stereotypic hand movements, with hand wounds resulting from these movements being more commonly reported in very young children.
- Approximately half of the girls and young women always use a wheelchair and the other half are able to walk with or without assistance. The common perception that most older girls and women are wheelchair bound was not what was reported, with there being no real variation in mobility according to age groups.
- While families reported the verbal communication skills of their daughters to be very limited, they described their daughters as regularly using eye contact and gesturing to communicate their needs and feelings.
- An assessment of the respiratory pattern known as autonomic monitoring has shown that breathing abnormalities occur almost universally in Rett syndrome². However, it may only be the more severe forms of hyperventilation or breath holding that are actually perceived by parents or clinicians. This seemed to be the case with only a quarter to a third of families describing hyperventilation and breath holding as occurring frequently on a daily basis. The behavioural characteristic of 'swallowing air' occurred more commonly among young women with Rett syndrome.
- Behavioural characteristics such as 'teeth grinding' and a 'scratching itch' were fairly commonly reported by families, particularly those with younger children. In contrast, 'vacant staring spells' appeared to be more a characteristic observed in older girls and women.

Recent research being conducted here and elsewhere has started to look at whether there is a relationship between particular behavioural characteristics and specific mutations on the *MECP2* gene³. Further development of this research through international collaboration over the coming years may begin to provide families with some expectations of the sort of behavioural characteristics they can expect in their daughters and consequently proactively assist them and health professionals with the management of these symptoms.

References

¹ Larsson G., B.Lindstrom et al. (2005). Rett syndrome from a family perspective: the Swedish Rett Center survey. *Brain & Development* 27: S14-S19.

² Julu P.O., A. Kerr et al. (2001). Characterisation of breathing and associated central autonomic dysfunction in the Rett disorder. *Archives of Disease in Children* 85(1):29-37.

³ Robertson L., S. Hall et al. (2006). The association between behavior and genotype in Rett syndrome using the Australian Rett syndrome database. *American Journal of Medical Genetics* 141B: 177-183.

Medical services

The questionnaire asked families to indicate the medical services they used and also asked them to evaluate how satisfied they were with the services they received. It is known that many girls and young women with Rett syndrome are in good general health, however some have multiple medical problems requiring ongoing medical treatment. Families indicated that 92% of girls and women attended an average of nine medical appointments in 2004/2005. Most commonly families and their daughters were visiting a general practitioner, dentist, neurologist, paediatrician or orthopaedic specialist.

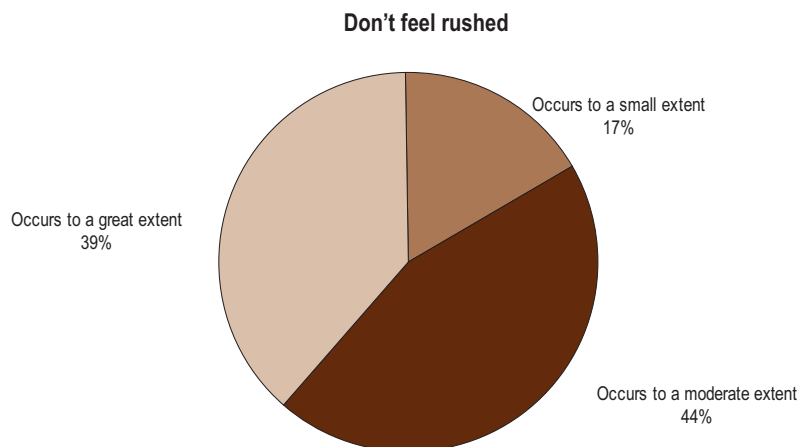
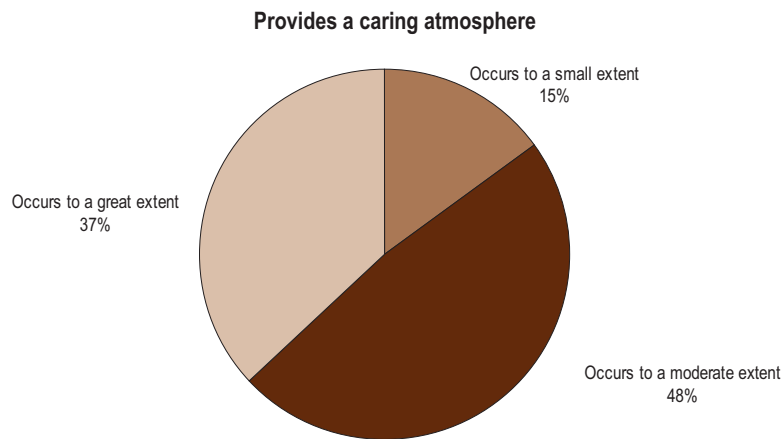
Families were asked to evaluate the care they receive from medical practitioners by answering 20 questions that make up a particular instrument called the 'Measure of Processes of Care' (MPOC). This particular measure of evaluation of services was developed by researchers from McMaster University in Canada following extensive consultation and input from parents of children with disabilities and is based on aspects of care that parents view as important¹. It aims to try to determine how satisfied parents feel about the extent to which they are treated respectfully; treated as partners in the medical care of their daughter; how coordinated the services are they receive; and how satisfied they are with the specific and general information provided to them about their child with a disability.

Families rate each question on a scale from 1 – 7 to indicate a behaviour occurred to a 'very great extent'(7) or 'not at all'(1). For each of the 20 questions in this measure, only a small number of families with daughters in the oldest age group answered the questions therefore they have not been included in any comparisons related to different age groups.

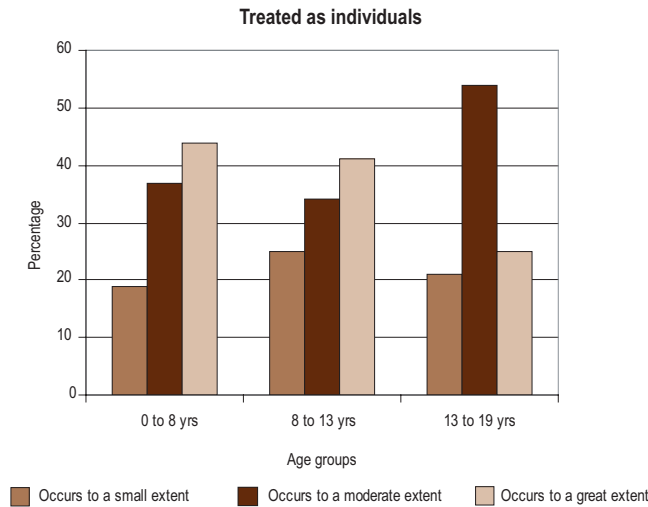


Respectful and supportive care

The questions that focused on whether families thought they were treated respectfully generally indicated that families thought this occurred to a moderate or great extent in most cases. Parents rated highest medical services that reflect the 'respectful' nature of the services they receive in terms of 'providing a caring atmosphere' (37% stating this occurred to a great extent), and providing them with 'enough time to talk so they don't feel rushed' (39% indicating this occurred to a great extent).

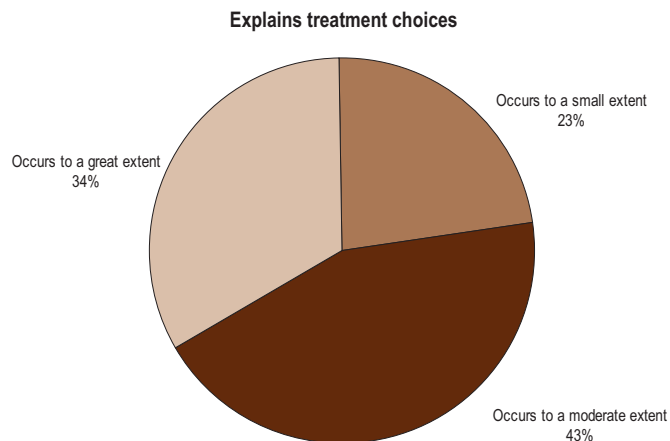


Over a third of families (34%) thought they and their daughter were always treated as individuals rather than as a 'typical' parent of a child with a disability, with 20% stating this occurred not at all or to a very small extent. There was some variation in age groups when families answered this question, those with younger children indicating this occurred more often 'to a great extent' than reported by families of adolescent daughters.



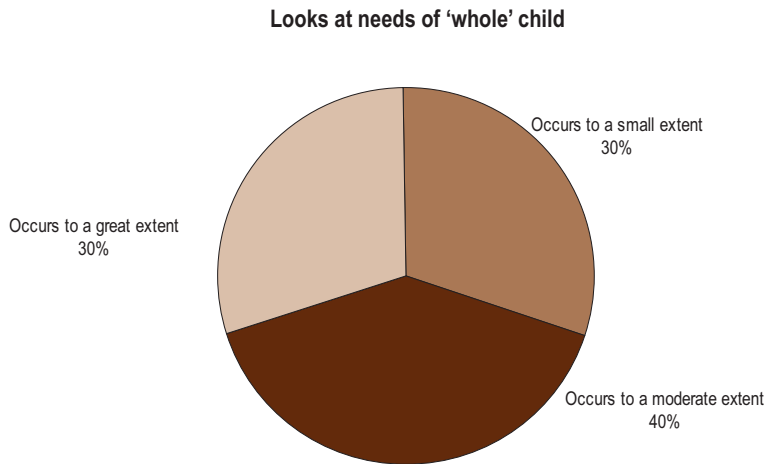
Enabling and partnership

Questions in the MPOC evaluation tool that focused on whether parents felt they were treated as partners by the medical professional involved in the care of their daughters, revealed that they thought this occurs to a moderate extent (approximately 40% of responses). For example, the question that asked whether 'treatment choices were fully explained to you' 43% of families said this occurred to a moderate extent, with 23% of families indicating this occurs to a small extent or not at all.

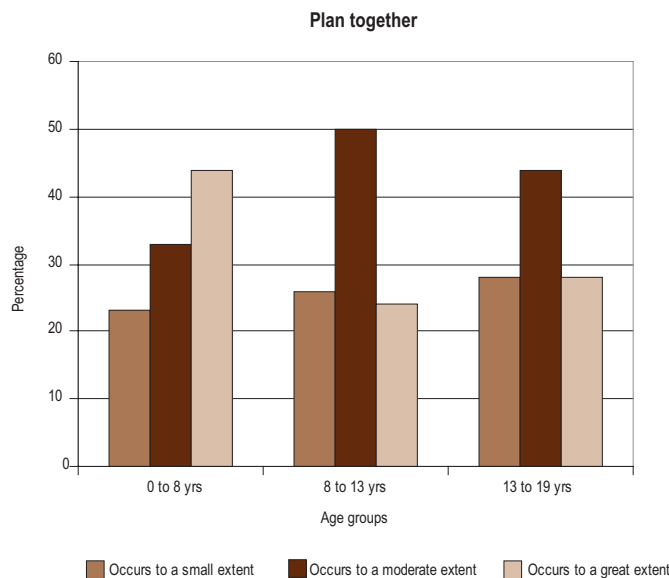


Co-ordinated care

Parents were asked to indicate how coordinated they thought the medical care of their daughter was, and again the most commonly used category by families was that this 'occurs to a moderate extent' (approximately 45% of responses). For example, the question that asked whether medical practitioners 'look at the needs of your whole child' 40% of families said this occurred to a moderate extent, with 30% of families indicating that this occurs to a small extent or not at all.

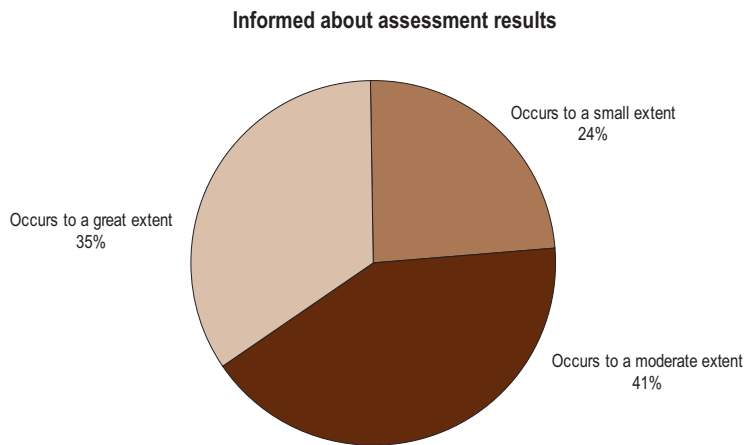


Families were also asked if they thought they had the opportunity to work with medical services to 'plan together so they are all working in the same direction'. Parents who had daughters younger than 8 years of age thought they had more opportunity to work together with medical professionals with regard to services and outcomes for their daughter compared to those with older children and adolescents.



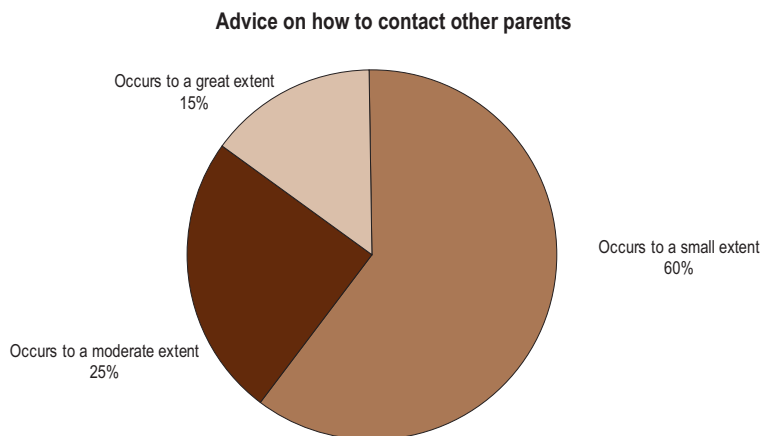
Provided with specific information

When families were asked whether they received specific information related to their daughter's assessment results most felt this occurred to a moderate or great extent, with 24% of families indicating that this occurred to a 'small extent or not at all'.

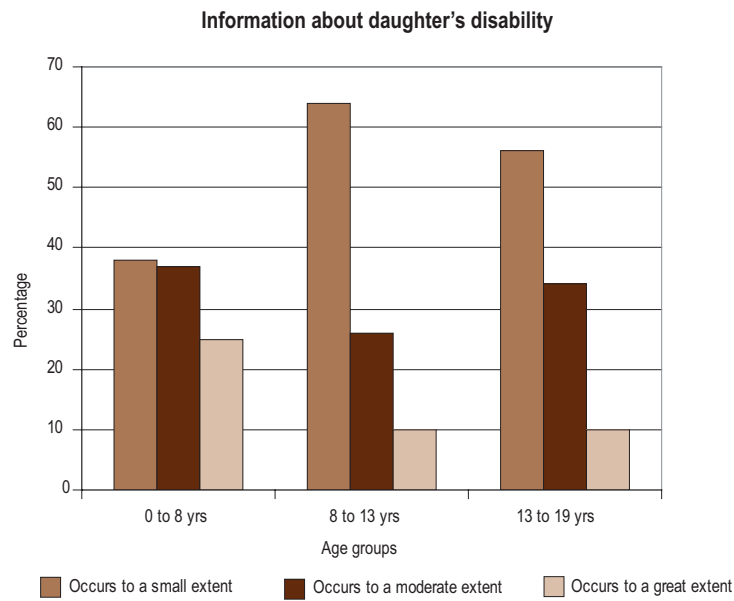


Provision of general information

Questions in the MPOC evaluation tool that focused on whether parents felt they were provided with general information by medical professionals related to the care of their daughters, rated this aspect of care very poorly. For most of the five questions related to this area, at least half of the families used the 'occurs to a small extent or not at all' category. For example, the question that asked whether 'they were provided with advice on how to get information or to contact other parents' 60 % of families said this occurred to a small extent if at all.



Families were also asked if they thought they were provided with information about their daughter's disability, such as causes or future outlook, by medical services. Again, parents who had daughters younger than 8 years of age thought they more often received this sort of information from medical professionals compared to parents with daughters with older children and adolescents.



As well as using numbers to rate and evaluate the medical services received, families were invited to make written comments with regard to their impressions of these services. While a number of families made very positive comments about their medical practitioners and services, a greater number of families expressed frustration and concerns about the quality of services they received and the general lack of information and expertise amongst the medical profession in relation to Rett syndrome.

'She receives excellent care and everyone fully understands and keeps themselves up to date with information on her condition'

'When she gets it, it is good, but we have to wait too long for things to be done, and then sometimes it is too late'

'Overall, her health care has been good, but I am constantly surprised at the ignorance of Rett syndrome amongst the broader medical community...I'm the one educating them usually'

'Our daughter has never received satisfactory medical attention as the environment is not congenial to her....she can demonstrate inappropriate behaviour in a medical practice and often refuses to get out of the car which means the Dr coming to her in the car park. A diagnosis is almost impossible and the treatment of illness guesswork on behalf of us all!!!!!!'

'I or my family provide information about Rett syndrome to the medical services, dental people and any other services up here.....I have only come across three people who know what it is'

'Health care is very fragmented with little or no interaction between providers....no 'whole child' or 'entire family' approach exists, nor any long term goals'

'....we have found that medical professionals seem to only go as far as giving you test results, diagnoses, prognoses, and then tell you to go out and find services yourself before you take your child home and care for them the best you can.....in terms of specialists' and GP's support staff...we find we can get what we need from them if we are 'nice' parents....they wield a fair amount of power and can make life difficult for parents if they are rubbed up the wrong way'



Families with children and adults with disabilities have an ongoing connection with the health system that provides services to meet their varying developmental and medical needs. The statement by one particular parent perhaps best summarises what families expect from medical services:

'... I strongly believe that all parents of Rett girls need a medical practitioner that: 1. is qualified and experienced in the treatment of disabled people 2. looks at the 'whole picture' of the girls medical needs 3. is available at short notice and low cost to the parents.'

For families with Rett syndrome it appears that they rate most highly the way in which they are treated by medical practitioners, that is, for the most part respectfully and as individuals. By far the greatest area for improvement according to families is in the area of the provision of general information, that is, information related to the prognosis and future outlook of their daughters, advice on how to contact other families and information about types of services available in the community. It is important to be able to measure how families perceive medical services, to provide information related to areas that need to be targeted to better meet families' needs.

Families with a daughter with Rett syndrome have made very clear the areas they believe need to be targeted by researchers, service providers and policy makers in order for services to adequately assist them with the many challenges of caring for a daughter with this disability.

References

- ¹ King S., P. Rosenbaum et al. (1996). Parents' perceptions of caregiving: development and validation of a measure of processes. *Developmental Medicine and Child Neurology* 38: 757-772.

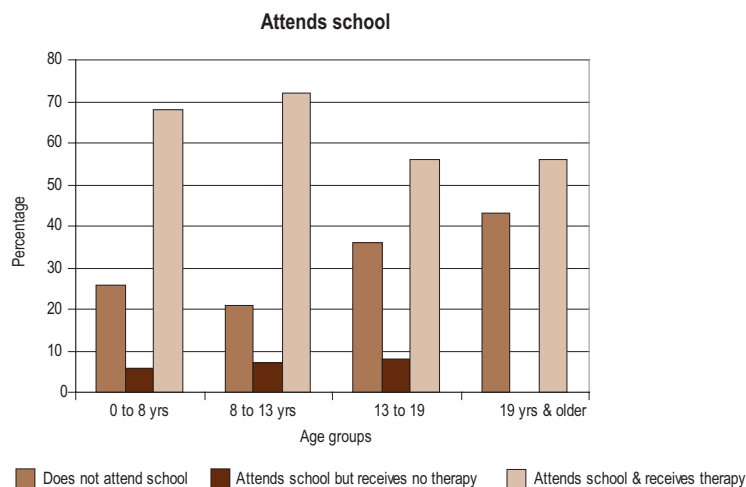
Educational, community & therapy services

A number of the sections of the questionnaire asked families to indicate the educational, community and therapy services they used and also asked them to evaluate how satisfied they were with the services they received. Families described therapy and community activities they had received and /or undertaken during the 2004/2005 period in different settings:

- Therapy at school.
- Therapy outside of school.
- Planned therapy activities at home.
- Recreational and day activities.

Educational placements and therapy received at school

Families were asked if their daughter attended school and of those who responded (189 families) 62% indicated their daughter attended school and received their therapy at school and 5% indicated their daughter went to school but did not receive therapy in the school setting. A third of families indicated their daughters did not attend school, with only 5% of girls being younger than school age.



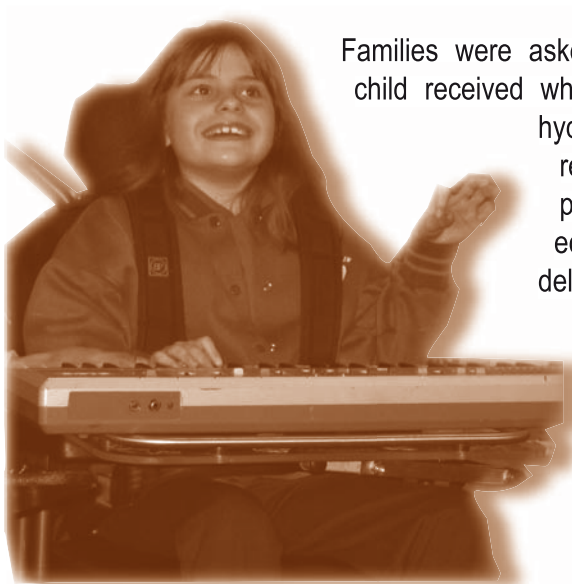
While it is expected that the younger age groups will have significant proportions of girls attending school, in the older age groups families indicated that over half of their daughters are still in an educational placement. The majority of girls and young women are attending a 'Development Support/Special Education School', with a small proportion attending mainstream schools. Almost 80% of families felt satisfied that the educational needs of their daughters were met in their current placements. However, some families expressed concern about the lack of support regarding communication devices and the 'struggle' to keep their daughters in the mainstream system with inadequate supports and infrastructure for children with a disability.

'It is such a great thing to have the support and help needed to care for our kids as part of the curriculum at no extra cost'

'Most therapy is integrated into school programs organised by therapists, but carried out by teachers and other staff...there is no such thing as one on one any more and hasn't been for years'

'I read and hear how other Rett girls are doing and I wonder if she is getting the best education...I was told that the speech therapist at school is so busy seeing the children with chewing and swallowing problems that communication is the least important'

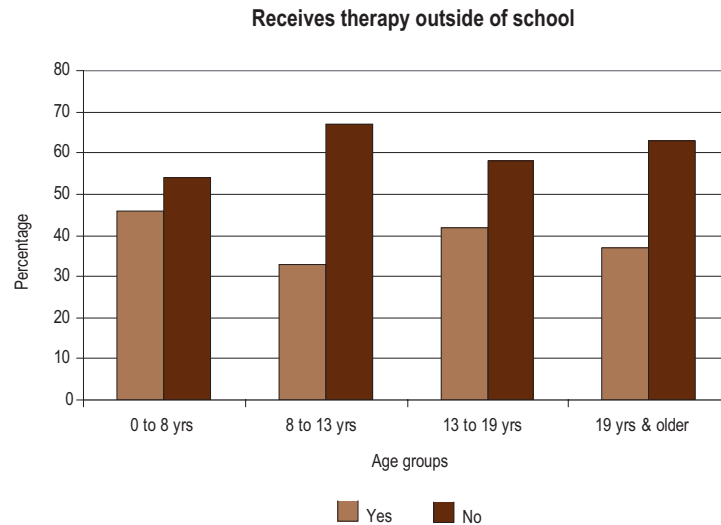
'No, we have arranged a placement at a special school for next year...we changed the placement because she was no longer happy in the mainstream setting... apparent from her behaviour....high anxiety and frustration leading to screaming and pinching.....I still think mainstream placement could work if there was a change in how the system worked eg more teacher/student support, more flexibility in how the system is implemented....our daughter has had some transition visits to her new school and seems to be very happy there...so I have to accept that maybe it is the best setting for her for now'



Families were asked to indicate the most common therapies their child received while at school, with physiotherapy, music therapy, hydrotherapy and horse riding being the most frequently reported. Most of these therapies are undertaken as part of the curriculum program offered by the 'special education environment', although they are usually delivered by teachers and educational assistants under the occasional direction of a therapist where appropriate. Of concern was the finding that only one parent indicated their child received any speech pathology and only 12 children were undertaking occupational therapy based activities.

Therapies received outside of school

Thirty nine per cent of families, that is 73 out of the 186 families who answered this question, indicated their daughter received therapy outside of school. As you would expect, proportionally, therapy received outside of school was greatest for the younger age groups as in most States of Australia government funding for services to children with disabilities is skewed towards younger children.



Physiotherapy and hydrotherapy were the most regularly received therapies outside of school, often being part of the day activity program or post-school options program for young women with Rett syndrome. However, some families commented that the regularity of these activities was very dependent on staff availability. It was also reported that after leaving school and entering adulthood, regular therapy services (outside of a day placement option) were *'non-existent'*.

'My daughter is now attending an adult training and support service, she is 'lucky' to get music therapy weekly in her program'

'Hydrotherapy booked by day program only when enough staff present'



A small number of families indicated they received therapy including physiotherapy, occupational therapy and speech therapy from a team of therapists. Most of these families were part of an Early Intervention Program with a disability organisation that provided these services in a kindergarten, day care, central playgroup or, more rarely, a home setting.

Other regular activities reported to be engaged in by girls and young women with Rett syndrome were horse riding from 'Riding for the Disabled' organisations and music therapy, both of these activities usually incurring some cost. A very small number of families indicated they accessed private physiotherapy, occupational therapy or speech pathology. However, these services remain extremely costly and are not sustainable for most families.

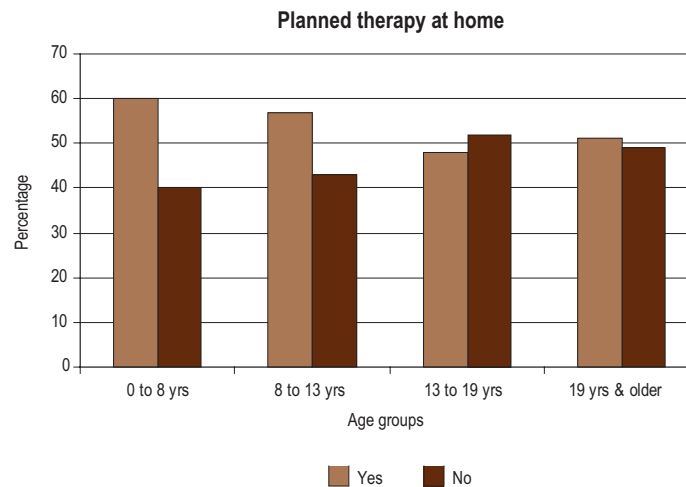
*'The cost is prohibitive and private insurance won't cover more than a month's worth...
quality of therapy is exceptional'*

'Don't have money to attend speechie/physio more often'



Planned therapy activities at home

Almost half of the families indicated they carried out 'planned' therapy activities at home, that is, where time is set aside on a regular basis for their daughter to have therapy at home. There was little variation in age groups as to whether this sort of therapy occurred at home, although families with daughters in the younger age groups indicated this sort of therapy is carried out slightly more often than occurs in the older age groups.



The most common types of therapy carried out at home included walking, stretches, time in standing frame, massages, prone lying, swimming and 'spa baths'. Almost all of this therapy was carried out by parents, grandparents and other members of the extended family. Very few families indicated the therapy was carried out by therapists visiting the home, although some families used carers and volunteers to do the therapy with their daughter. Many families also indicated the therapy is incidental and not 'planned', and is part of their daughters' everyday routine.

'Most of the therapy I do with my daughter I try to make it fun...she loves music and singing and we do actions with our hands...giggling therapy is good too!'

'Therapy at home is incidental...but incidental all day long!'

'We complete a range of therapies at home however this is not planned or scheduled...it is the way we handle and deal with our daughter'

'It is hard to say how often...depends on how my daughter feels...some days more is done, when others nothing is achieved'

Recreational and day activities

Fifty four adolescents and young women were described as being part of a regular day activity program outside their home, with most attending a 'Day Activity Centre' or 'Post-School Options' program.

Common activities reportedly occurring in these programs were community outings, cooking, arts and crafts, massage therapy, music therapy and hydrotherapy.

Almost 70% of families indicated they were satisfied that their daughter's needs were being met in their current day activity program, with 20% stating they thought the needs of their daughter were not met. A small proportion was unsure whether these programs met their daughters' current needs.

'As best they can be in a small rural community with limited resources'

*'Lack of therapy input is disappointing...having been trained to use a communication device before leaving special school, this is rarely used by instructors in day program
.....they lack training in communication aids use'*

'Not really...spends long hours alone and bored'

A common area of concern was the lack of use of communication aides in these environments and the paucity of specifically tailored programs. However, it appears most families were resigned to the fact that the current day activity placements of their daughter was their only real option.....'*nothing else available so have no choice'*.



Evaluation of therapy services

Therapy services in Australia that practice contemporary models of service delivery embrace a model known as 'family centred practice'. A family centred approach to therapy is a type of service that:

- Emphasises a partnership between parents and therapists.
- Recognises parents as the experts in the care of their child.
- Focuses on the family's role in decision making about their child.
- Fosters mutual respect between families and staff as they work together to achieve desired outcomes for the child and family.

One hundred and seventy five families and their daughters received therapy in the 2004/2005 period. Families were asked to evaluate the care they received from therapists by answering 20 questions that make up the previously described instrument, the 'Measure of Processes of Care' (MPOC).

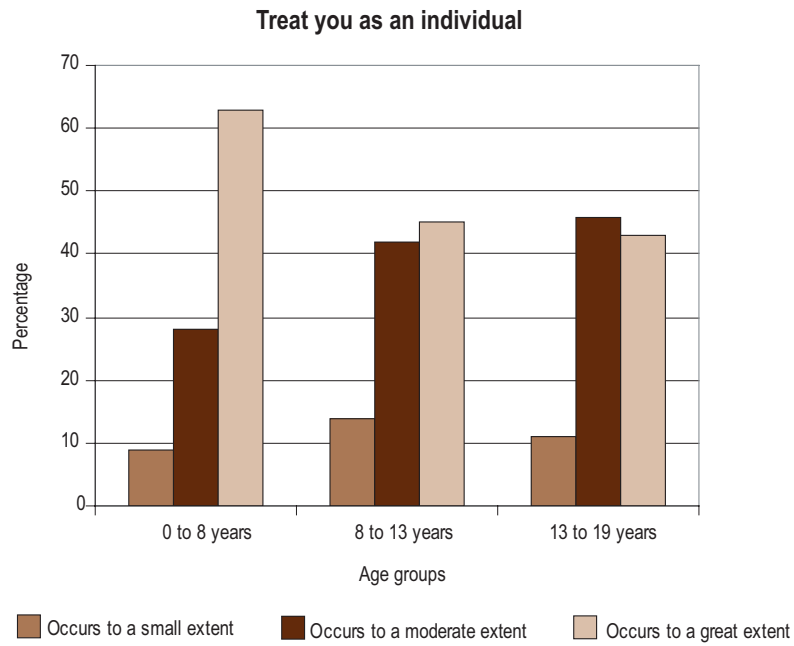
For each of the 20 questions in this measure, only a small number of families with daughters in the oldest age group answered the questions therefore they have not been included in any comparisons between different age groups. As well as using numbers to rate and evaluate the therapy services received, families were invited to make written comments with regard to their impressions of these services. Some of these comments have been included where appropriate.

Respectful and supportive care

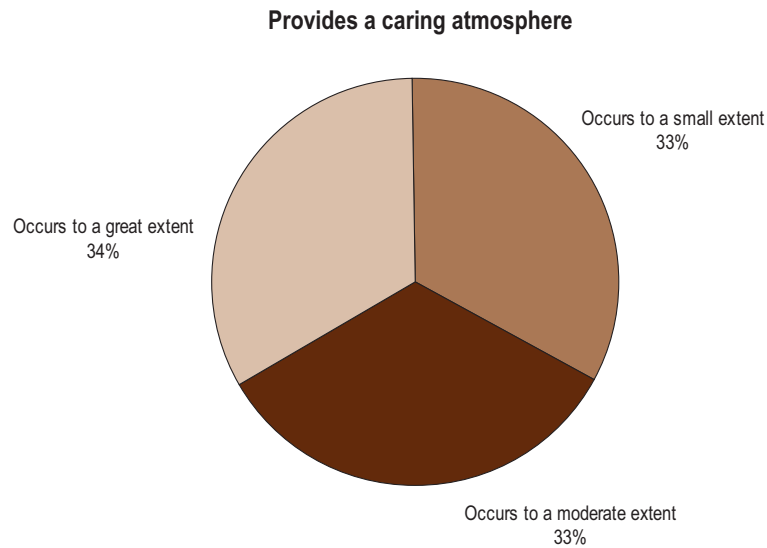
The questions that focused on whether families thought they were treated respectfully and viewed as individuals and equals by therapists generally indicated that families thought this occurred to a moderate or great extent.

Parents rated being treated as individuals (rather than as a 'typical' parent of a child with a disability) highly, with almost 50% of families indicating this 'occurred to a great extent'. There was some variation in age groups when families answered this question, those with younger children indicating this occurred more often 'to a great extent' than reported by families of adolescent daughters.





For questions related to respectful and supportive care, families rated services slightly lower in terms of 'providing a caring atmosphere' (34% stating this occurred to a great extent), and providing them with 'enough time to talk so they don't feel rushed' (31% indicating this occurred to a great extent).



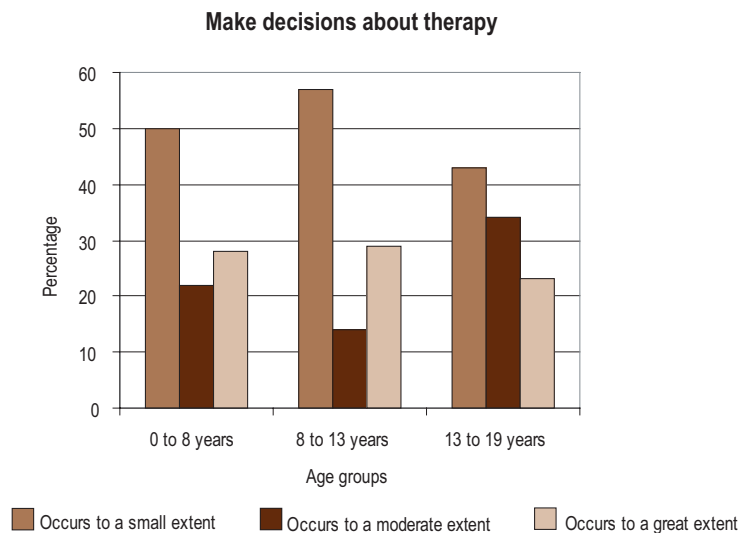
'The therapists at my daughter's early intervention program are fantastic...I really try and talk to them as much as possible....the more involved I get the more they offer to my daughter.....they have always been there when I have needed them'

'I generally feel that we are treated just like a time waster at times.....Not all but a majority seem to use this regional centre as a stepping stone to a capital city position and don't take a great interest in us'

Enabling and partnership

Parents rated poorly the questions in the MPOC evaluation tool that focused on whether they felt they were treated as partners by the therapy professionals in the care of their daughters, with about half indicating this occurs to a small extent or not at all. For example, for the question that asked whether 'treatment choices were fully explained to you' 48% of families said this occurred to a small extent, with 25% of families indicating that this occurred to a great extent.

When asked if they were provided with opportunities by therapists to make decisions about therapy, about half the families said this occurred to a small extent if at all, with those families with younger school aged children reporting they rarely have this opportunity. Many families commented that they rarely saw or spoke to a therapist, particularly if their child is in a special education school, where most of the therapy is carried out by teachers and/or educational assistants.



'There is not much parental involvement in adult services'

'Due to her being at school I rarely see the therapists or hear from them...if I have any queries they will react appropriately but apart from that there is no contact'

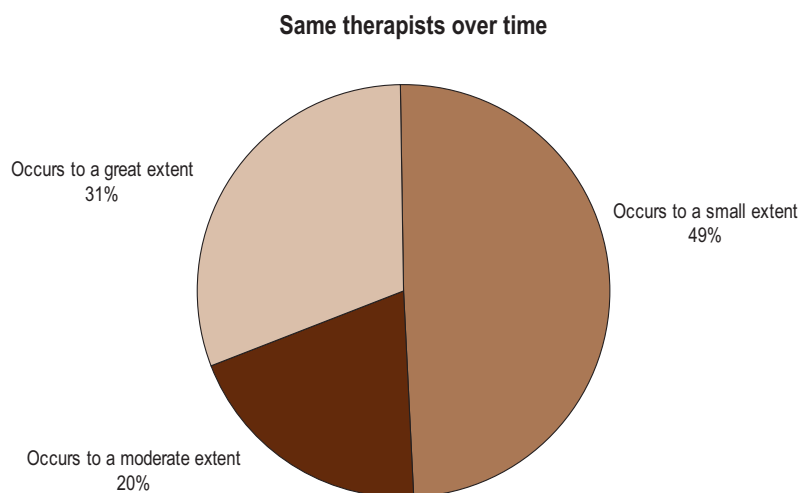
'As parents we feel frustrated with the lack of communication from therapists...they contact the schools but not the parents...have spoken to them numerous times with not much success'

Co-ordinated care

Parents were asked to indicate how coordinated they thought the therapy care of their daughter was, and their responses to the questions in this section were particularly variable. For example, when asked whether they 'plan services together so everybody is working in the same direction' 44% of families said this occurred to a great extent, and 19% of families indicated that this did not occur at all.

The large number of families rating this question highly is likely to be due to the fact that most educational placements providing a service to a child with a disability, particularly special education placements, have an annual Individual Education Planning (IEP) meeting. The IEP brings together teachers, families and therapists to set goals for the student for the year.

For other questions that focused on how coordinated therapy care is, families mostly used the 'occurs to a small extent or not at all' category. Nearly 50% of families indicated they rarely had the same therapist over time, and almost two thirds indicated the therapy they received almost never considered the needs of their 'whole' child.



Look at needs of whole child



'Living in the country consistency of services is often hampered by constant changes in personnel including long periods of no service.....the therapists are always overworked and I have never really been satisfied with the level of services that my daughter receives'

'Whilst having the health professionals at school is convenient, I would have to say it leads to some remoteness in that we only formally meet once a year to hear about my child's progress'

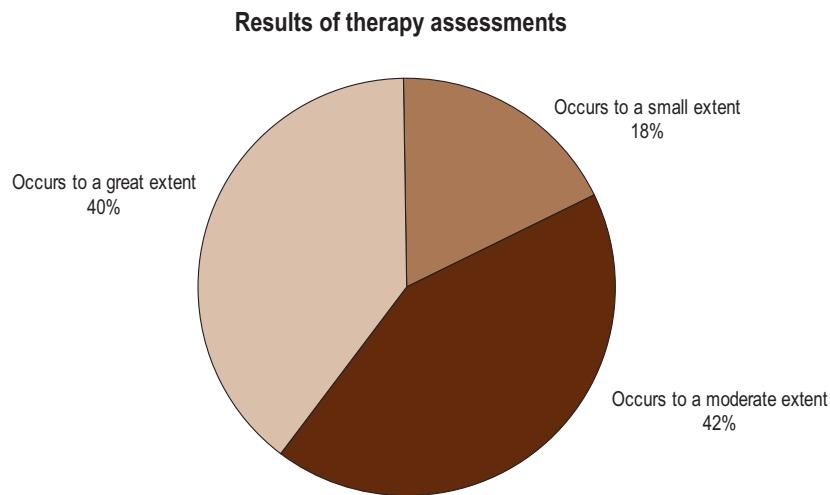
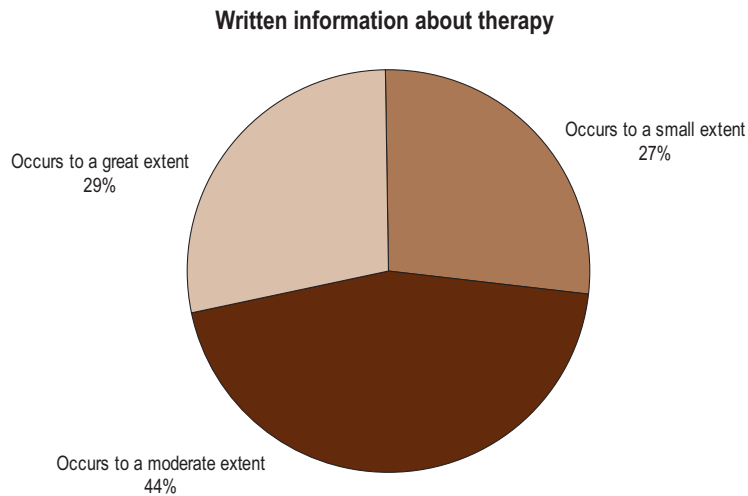
'Aside from physiotherapy I am appalled at the level of service and lack of consistency....in the last 18 months we have had (I think) four OT's, 3 Speech Path.... and between them all our daughter has seen them all about 2-3 times....the service is very poor and she hardly has any actual treatments...visits seem to be all talk and no action and pretty much if I think of something then I chase them for appointments'

'I have HUGE issues with the teamthe therapists only stay 1 to 6 months so then the next person comes, starts the 'get to know you stage' – doesn't put anything into practice, leaves and then the whole process starts again...'

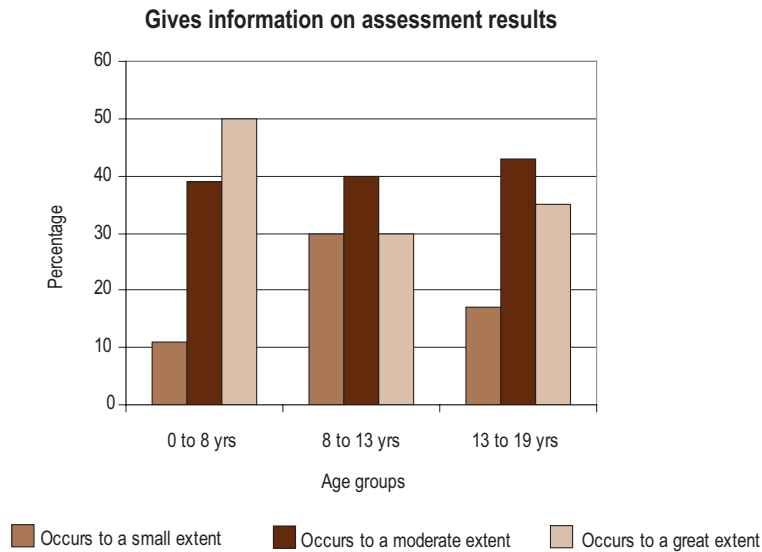


Provided with specific information

When families were asked whether they received specific information related to their daughter's assessment results or written information about therapy most felt this occurred to a moderate or great extent.



When looking at the responses of families of daughters in different age groups, it is clear that parents with young or adolescent daughters appear to be receiving information on assessment results more consistently than those with daughters in the middle primary years.

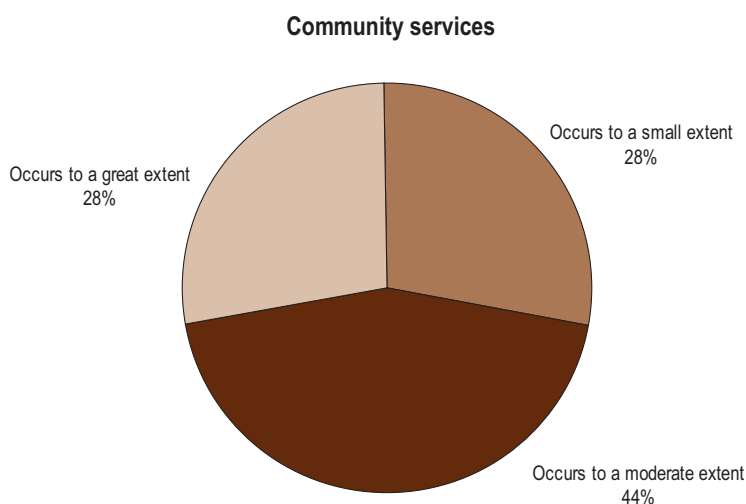


'Overall I've been impressed with the commitment the various therapists have shownthey have all either been aware of Rett syndrome or have made serious efforts to learn about it and used that information to tailor their programs'

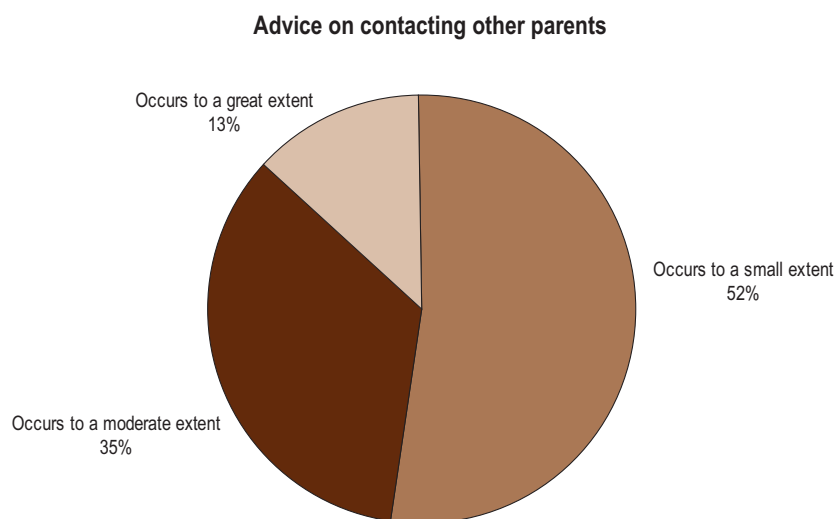
'This is such an important area...we are very happy with the service our daughter is currently receiving....more resources would be helpful, but everyone is doing the best they can with limited resources'

Provision of general information

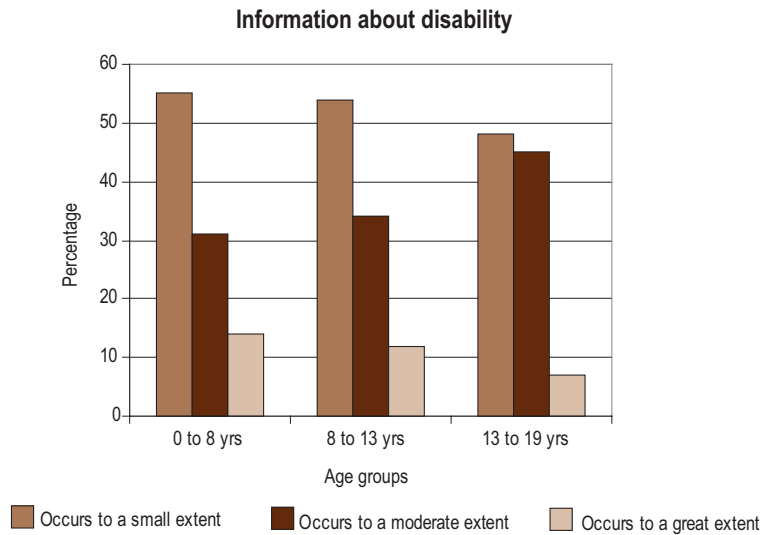
Questions in the MPOC evaluation tool that focused on whether parents felt they were provided with general information by therapists related to the care of their daughters, resulted in families rating this as the most poorly done aspect of the services they received. For all but one of the five questions related to this area, approximately half of the families used the 'occurs to a small extent or not at all' category. The exception was the question that asked whether therapists offered families information about services available in their community, and most of the parents indicated this happened to a moderate to great extent.



The question that asked whether therapists provided them 'with advice on how to get information or to contact other parents' 52% of families said this occurred to a small extent if at all, with only 13% of families indicating that this occurred to a great extent.



Families were also asked if they thought they were provided with information about their daughter's disability, that is, how it progresses and the future outlook. Unlike with some other questions, there was no great difference between families who have daughters of different ages with Rett syndrome, all reporting this was information that, on the whole, they rarely received from therapists.



'The biggest outcry is they (the teachers) get very little assistance from anywhere else, only what we can find on the internet or provided by me...no one shows much interest in it'

'Did not really know what Rett syndrome was or dealt with before'



'As I said before I know more about Rett syndrome than most people working with my daughter in this area....they tend to treat the current problem not the whole disability'

'... 95% of therapists have never heard of Rett so I have to explain this to them and even then their ideas of therapy do not match my daughter's abilities or needs. I stopped going because I found it insulting and a waste of my time'

Therapy and therapy services are a large part of the lives of families with a daughter with Rett syndrome. Some families made very positive comments about their therapy services, particularly those with younger children. However a greater number of families expressed frustration and concerns about the quality of services they received and the general lack of information and expertise amongst the therapy professionals in relation to Rett syndrome.

Of particular concern to researchers, policy makers and service providers should be:

- The lack of coordinated care provided to families and their daughters due to high turn over of therapy staff, and the limited suitably trained staff particularly in country areas.
- The limited communication between therapists and families in relation to the care of their child, families rating particularly poorly their sense of being treated as a partner in their child's care.
- The lack of therapy and other suitable supports and infrastructure in mainstream schools for children with disability.
- The very limited focus given to communication and communication aides in girls and young women with Rett syndrome.
- The significant decrease in therapy services as children grow older and move into adulthood.
- Families' need to receive much more general information related to their daughters' disability, particularly prognosis and future outlook.
- The need for the whole family to have the opportunity to receive information and support and advice on networking with other families.

In paediatric therapy and rehabilitation it is known that a family centred approach to services, results in greater parental satisfaction with services, better parental psychosocial well-being and better developmental outcomes for the child or young person with a disability^{1,2}. Unfortunately, from the feedback obtained from families it appears that therapy services provided to girls and young women with Rett syndrome have much work to do to ensure that the rhetoric of family centred services becomes much more of a reality in clinical practice.

References

¹ King G.A., S. M. King et al. (1996). Interpersonal aspects of care-giving and client outcomes: a review of the literature. *Ambulatory Child Health* 2: 151-160.

² King G.A., S. M. King et al. (1999). Family-centred caregiving and well-being of parents of children with disabilities: linking process with outcome. *Journal of Pediatric Psychology* 24: 41-53.

Common areas of concern for families

Families with daughters with Rett syndrome are continually faced with new and ongoing challenges. Common areas of concern relate to puberty, mealtimes and nutritional intake, sleeping and respite. This section of the report highlights how families have answered questions related to these areas in the 2004/2005 questionnaire.

Puberty

Sexual development

Three quarters of families reported that they did not think there was anything unusual or different about their daughters' sexual development than what would be expected for her age.

The comments made by the remaining 47 families were very varied. Some of the families thought their daughters displayed 'slower sexual development' and had 'child-like bodies' whereas others reported they seemed to be much 'more developed' than other girls the same age. However, the most commonly reported unusual aspect was the very early development of pubic hair without any of the other associated aspects of sexual development.

'Her pubic hair developed but didn't develop any other way eg breasts, thought this was unusual as started getting pubic hair when 10 years'

'She has had pubic and underarm hair since she was 4 but no other signs of puberty yet'

'Presence of pubic and auxiliary hair at age of 7'

Menstruation

Exactly half of the families who answered the question on menstruation reported that their daughter had started menstruating, and 72 of these families were able to provide the age at which this occurred. The average age at which girls started their period was 13 years, with the youngest age reported being 9 years and the oldest 22 years.

Almost 60% of those families whose daughter has begun menstruating reported problems associated with her period. The most commonly reported symptoms were pain and agitation with over a third of families stating they thought their daughters' seizure activity increased just before or during menstruation.

Some families reported that their daughters had particularly 'heavy bleeding' while others commented their daughters' periods were very irregular and might only occur once or twice per year.

'Our daughter is very miserable with her period, she eats less and sleeps through the day. Two days before her period starts she has increased myoclonic activity and frequent drop attacks. She appears to be in severe pain for a couple of days and has more nights of hyperventilating than normal'

'Ovulation caused cramps and pain, made her very agitated, had many seizures'

'She gets very agitated before her periods and usually does get very unsteady on her feet...she will sit herself down on the floor'

About half of families whose daughters had begun menstruating reported they used medication to manage menstrual periods. Six families stated their daughters had had surgical procedures related to their periods, four of the procedures being a hysterectomy. Depo-Provera injection was the most commonly reported medication used to control the menstrual cycle along with a range of different brands of the contraceptive pill. Some families reported the only medication they used was paracetamol or ibuprofen to manage their daughters' pain during menstruation.

A number of suggestions for families related to menstruation have been included in the latest August 2006 'AussieRett Connect' newsletter (pictured below). Gynaecologists working with girls and young women with disabilities report that most will pass through menarche at the usual time and go on to menstruate with the same regularity as their peers¹. This has been the experience of the majority but not of all families with a daughter with Rett syndrome. Medical practitioners need to be aware of this and provide additional support and information to families when required.

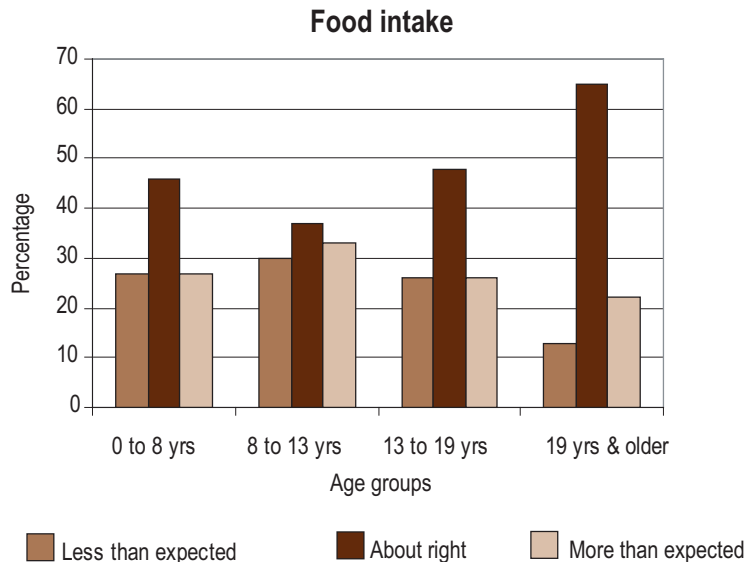


Meal times

It is known that feeding difficulties in Rett syndrome are common. The causes are complex and not fully understood with swallowing difficulties, decreased ability to eat and drink independently and the presence of other gastrointestinal symptoms all being part of the puzzle. For some, but not all, this may result in loss of adequate nutritional requirements and impaired growth and 'failure to thrive'. Severe feeding difficulties may result in the use of enteral nutritional support (ENS). Occasionally this involves the use of nasogastric tube feeds when the problem is considered to be relatively short term with the use of percutaneous endoscopic gastrostomy (PEG) feeding being a more permanent support.

Meal times and nutritional intake

The 162 families, whose daughter did not have a PEG or nasogastric tube, were asked to describe the quantity of food that their daughter eats. About half of the families indicated that they thought it was 'about right for someone of her size'. Similar proportions of girls were described as eating 'less than' or 'more than' expected for someone of their size. There was little variation between age groups with the exception of young women who were more likely to eat what would be 'about right for someone of her size'.



About one third of families reported that their daughter had no difficulties eating any type of food, however most families indicated their daughters' food needed to be either mashed, pureed, finely chopped or cut into bite size pieces. The most commonly required preparation for food was for it to be cut into bite size pieces, with this being reported by about half the families.

All families were asked to indicate their feelings about whether their daughters' intake of fluid is adequate. One third of families had no concerns about their daughters' fluid intake, however a third of families were constantly or frequently concerned. These families tended to have daughters in the younger age groups.

FLUID INTAKE	%
I don't have any worries about this	33
There are occasional periods when I worry (monthly)	33
I frequently worry about her liquid intake (weekly)	18
I constantly worry about her liquid intake	16

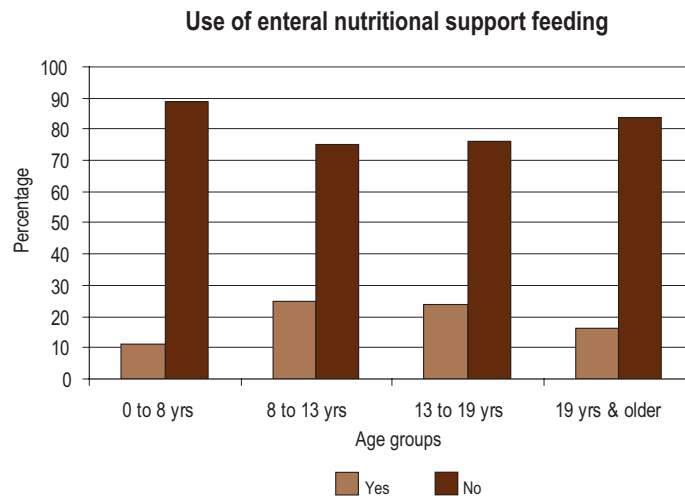
Families were asked how long it usually takes for their daughter to have a meal, and the most frequently reported time was 30 minutes with the average length of time being 25 minutes. The longest length of time reported was 2 hours.

A way of classifying feeding difficulties has been described that reports the degree of difficulty according to the time it takes for feeding: mild (15 minutes), moderate (15-30 minutes) or severe (longer than 30 minutes)². Using this classification system, families reported that 13% of their daughters had mild feeding difficulties, 47% moderate feeding difficulties and 40% could be classified as having severe feeding difficulties.



Percutaneous Endoscopic Gastrostomy (PEG) feeding

PEG feeding is being used more often in girls and young women with Rett syndrome as a way of ensuring adequate nutritional intake. Forty families reported they used either a nasogastric tube or PEG for feeding, with it being more common in the middle age groups than in young children or women with Rett syndrome.



To date, there has been little research investigating the impact of PEG feeding in Rett syndrome. A study looking at the impact of PEG feeding on the quality of life of carers of children with cerebral palsy found that they reported a decrease in feeding times, increased ease of administering medication and reduced concern over the child's nutritional status³.

The most frequently reported time taken to feed their daughters was 30 minutes both for those families whose daughters did or did not have a PEG. The maximum length of time reported for a PEG user was 60 minutes which was considerably less than the 2 hours for those without a PEG. However, in regard to other aspects of mealtimes and nutritional intake, families whose daughters are fed using a PEG described many advantages and few disadvantages.

Some of the advantages of a PEG reported by parents were:

'....gives us peace of mind....our daughter is well hydrated, happier and healthier'

'....knowing daughter is getting adequate food and fluid intake, decreases worry and stress'

'....saved her life...is a godsend'

'....no worry about aspirating...going on holidays much easier to take supplies and can hook up anywhere even in car'

'....well hydrated, particularly when unwell...ease of administering medication...able to help decrease 'GAS' in stomach...decrease pain'

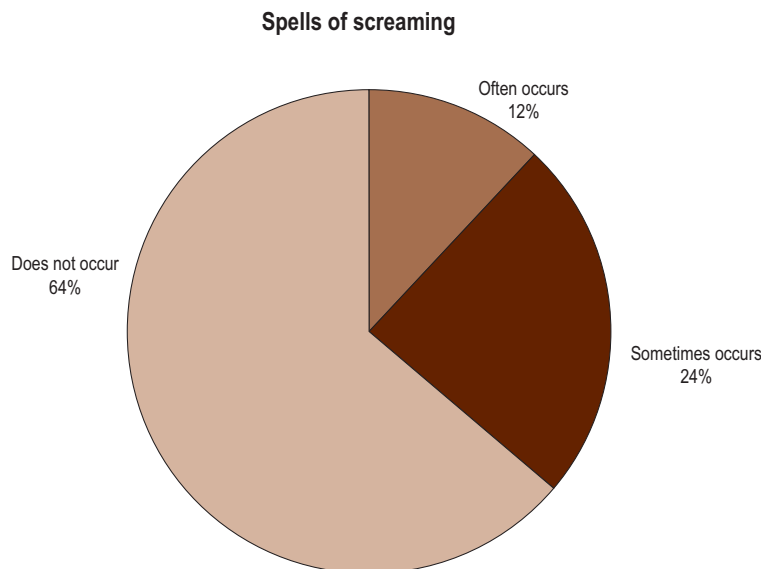


Of the disadvantages reported the most common was 'reddening' or skin breakdown of the site and the limitations it places on use of respite *'unable to find many places who will take people with PEG for respite either in home or out of home'*.

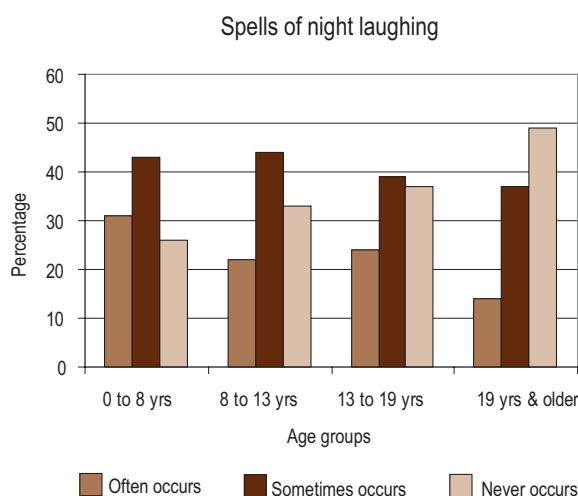
sleeping

Sleep problems are a recognised feature of Rett syndrome. They may take the form of waking in the middle of the night giggling or laughing, or a tendency to sleep longer during the day. Almost 80% of families reported that their daughter had some problems with sleeping. About 40% of girls and young women were said to wake occasionally, with 22% being described as waking frequently or constantly at night. Twenty per cent of families described their daughters as having a close to normal or normal sleeping pattern.

Some of the commonly reported behaviours related to sleeping in Rett syndrome include spells of screaming and/or laughter at night, crying at night and frequent napping during the day. Crying at night was not a commonly reported behaviour by families, with 65% indicating this never occurs and 7% stating this is often true for their daughter. Similarly, spells of screaming at night were not described by families as being a frequent occurrence, with 64% of families reporting this never occurs.



Spells of laughter during the night (night laughing) appear to occur more frequently than spells of screaming, with over 60% of families indicating that this frequently or sometimes occurs. There was some variation in this behaviour with age, being less common in young women with Rett syndrome.



About a quarter of families reported they use some medication to assist their daughter to sleep at night, some of this medication also being used to control seizure activity. However for most families, assisting their daughter to sleep was done by reassurance and comfort, with a few families using aromatherapy and pieces of equipment such as 'symmetrisleep'. Some of the comments related to sleep made by families were:

'always very restless sleep...vocalising, scratching face....no medications....hands tucked securely under sheet to restrict movement, wears socks as gloves to prevent scratching.....turned 2-3 times per night'

'wakes during the night ...difficult to settle ...often takes a long time to go to sleep... will hyperventilate and throws body aroundno treatment ...have tried to use an oil blend for peaceful sleep (aromatherapy)'

'she quite often wakes during the night and looks out the window for hours and then sleeps for hours during the day....no medication...she just does her own thing'

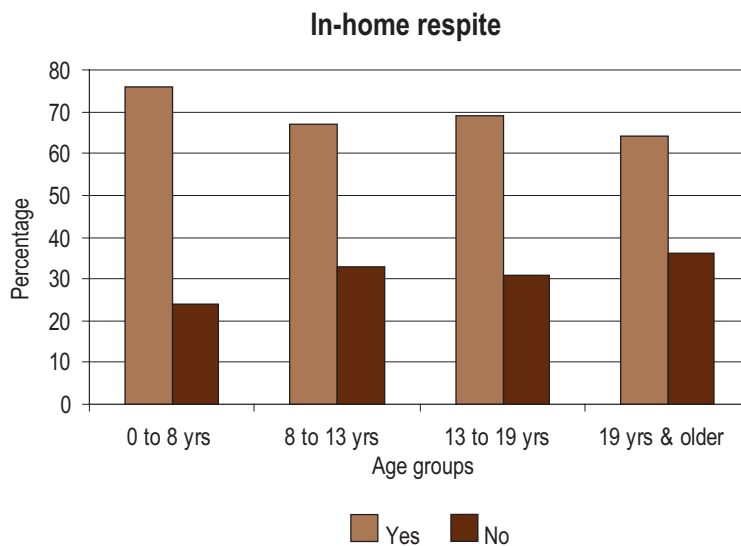
'no current problems with sleeping since using symmetri-sleep kit which was and is used to prevent spinal curvature...her physio was correct in thinking if the movement was stopped during sleeping then she may not have the nightmares/terrors by waking up scared'

Respite

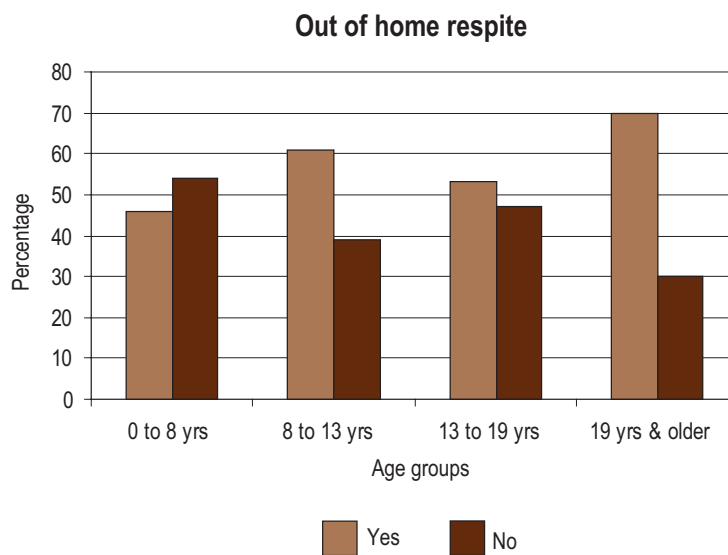
Many families with daughters with Rett syndrome receive help and support from other family members and extended family. However, the use of more formal respite care and services is important for all families who are caring for a family member who has a long term disability. Almost all families (78%) indicated they had used formal respite since January 2004, with a small number commenting that they had never received or requested respite care.

Of those families who are users of formal respite services, two thirds reported they used in home respite services with there being little variation across age groups. The often common expectation that the use of in home respite support decreases as children get older was not the case for families with daughters with Rett syndrome.

Almost 60% of these families stated they were required to contribute to the cost of this care; the most common cost being \$2.50 per hour, the average cost being almost \$7.00 per hour and the maximum cost contribution being \$30.00 per hour. Families stated they received in home respite from a variety of sources, including local councils, disability respite agencies, religious organizations and Silver Chain. Some families were part of the 'brokerage' system for in home respite where they are given the money to pay for a carer to come into the home. Families commented that while this was fine in theory, the availability of skilled and suitable carers was very limited: *'we are provided with the funding....we organise the carer ..not an easy task!'*



Almost 60% of families using formal respite care indicated their daughter had been in overnight care outside of the home. Again about 60% of these families stated they were required to contribute to the cost of overnight care; the most common cost being \$15.00 per night, the average cost being \$36.00 per night and the maximum cost contribution being \$156.00 per night. Families stated they received this care from a variety of sources: disability respite agencies, religious organisations, carers' homes, and Interchange families. There was some variation across age groups, with the greatest proportion of users of out of home respite being young women with Rett syndrome.



Researchers working on the Australian Rett Syndrome Study recognise the importance of formal respite services for families. While some information has been gathered about respite use that maybe of value to families, what is not known is how satisfied families are with the respite services they receive.

For example: how much respite families perceive that they need, are they receiving; how many families are limited in their use of respite because of cost; and how many families are having to use extended families and friends for in home support and overnight respite services because more formal supports are not readily available to them.

These are important areas to focus on in future work related to respite services for families with daughters with Rett syndrome.



Families raising daughters with Rett syndrome have highlighted their need to have access to ongoing and contemporary information with regard to their daughters' disability. About half of families have indicated they have made use of the Australian Rett Syndrome Study website www.ichr.uwa.edu.au/rett/aussierett and the International Rett Syndrome Association's website www.rettsyndrome.org. Families commented that they found both sites *'informative and useful'*. However, many families reported being too time poor to spend time on the computer (*'who has time to get on the net? ...are you kidding??'*) and other families indicated they did not own a computer. One of the aims of the Australian Rett Syndrome Study is to be available to families who are seeking information and have questions, and Dr Helen Leonard and members of the team are always willing and available to receive telephone calls and emails from families and health professionals (contact details are contained in the front of the report).



<http://www.ichr.uwa.edu.au/rett/aussierett>

References

- ¹ Atkinson E., M. Bennett et al. (2003). Consensus statement: menstrual and contraceptive management in women with an intellectual disability. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 43: 109-110.
- ² Morton R.E., R. Bonas et al. (1997). Feeding ability in Rett syndrome. *Developmental Medicine & Child Neurology* 39: 331-35.
- ³ Sullivan P., E. Juszczak et al. (2004). Impact of gastrostomy tube feeding on the quality of life of carers of children with cerebral palsy. *Developmental Medicine & Child Neurology* 46: 796-800.



PART 2

'Current research and publications'



Current research

The Australian Rett Syndrome Study has, over the last decade, produced a plethora of work that has helped families, health professionals and other researchers begin to understand more about the complex condition that is Rett syndrome. This is illustrated by the many presentations of this work at conferences in Australia and other parts of the world and the publication of research results in several internationally renowned journals.

This section highlights some of the recently completed and current research.

Genetics

One component of the research work undertaken by the Australian Rett Syndrome Study over the last few years has involved exploring the association between the severity of the level of symptoms and particular mutations (ie mistakes or errors) in the *MECP2* gene. This is called the investigation of 'genotype phenotype relationships'. Since the last report was compiled the study has produced twelve papers relating to this topic in the international medical literature¹⁻¹³.

By the end of 2004 almost 90% of participants in our study had had genetic testing undertaken with the finding of a *MECP2* mutation in 75%⁸.

How mutations occur

All DNA is made up of strings of chemical "text" represented by the letters A, C, G and T. For example, a strand of DNA (without a mutation) could be represented by:

AAG ACU UAA GAG

The letters are read in groups of 3, and each group is translated into a particular amino acid. It is essential that the right amino acids are translated, so the letters have to be in exactly the right order. Mutations happen when the sequence of letters are altered (or mutated) in some way. There are several types of mutations that can occur. Some examples are:

i) Missense mutations: these occur when the wrong letter is substituted into the sequence. For example,

AAC ACU UAA GAG

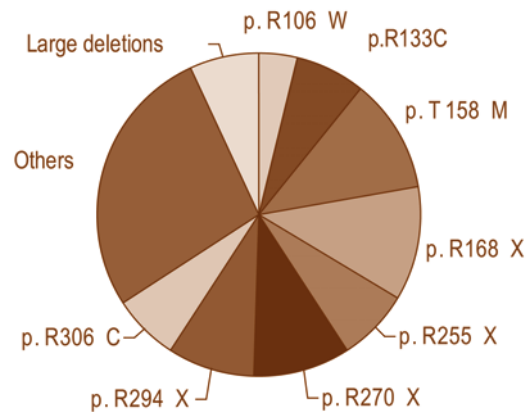
Here, there is a C where there should be a G, and a different amino acid is made at that point.

ii) Nonsense mutations: here, as with missense mutations, an incorrect letter is substituted in the sequence. However, the result is a group of 3 letters that represent a "stop signal", so the rest of the gene segment is not translated into amino acids.

AAG ACU UAG

Here, there is a G where there should be an A, and the stop code "UAG" is produced. The codes UAA and GAG are not translated, and the corresponding amino acids are not made.

In the Australian population several mutations known to occur commonly in Rett syndrome were present in the following proportions illustrated in the diagram below.



As mostly found elsewhere in the world, the commonest mutations were the missense mutation p.T158M and the nonsense mutation p.R168X⁸.

In some of our studies we have measured the clinical severity of Rett syndrome by using information provided in the questionnaire, for instance about mobility, seizures, and scoliosis^{1,2,3}. We have also been able to measure functional ability from questions families have filled out. We have then looked at the associations between clinical severity and functional ability and the different mutations^{2,3}. In 2003 we carried out a study in association with groups from Japan and from the Institute of Medical Genetics in Cardiff, Wales. We found that the p.R133C mutation was likely to have a milder effect such that girls and young women with this mutation were more likely to be less severely affected². They were more likely to be able to walk and some had a little speech.

On the other hand we found that some of the nonsense mutations, as might be expected from the mechanism by which they operate, were associated with greater clinical severity^{3,6}. However we discovered that these findings did not apply to all nonsense mutations and we found that one, the p.R294X mutation, was quite mild and associated with much better mobility³. Most girls with this mutation were able to walk. Later, when we were exploring the relationship between genetic mutation and onset of scoliosis, we also found that with this mutation scoliosis was less likely to occur or had a later onset¹¹.

Our early studies were followed with another collaborative study where we combined the Australian data with that provided in our international study, InterRett⁴. This provided the opportunity for even larger numbers and better ability to detect associations. In this study we looked at development and progress in the first year of life in relationship to particular mutations. The patterns we found mirrored our earlier work on clinical severity. That is, early development was most likely to be abnormal in children affected by those mutations we had already found to be associated with increased clinical severity. On the other hand, early mobility was likely be better in those girls affected by mutations we had already shown to have a milder clinical picture such as the p.R133C or p.294X mutations.

As well as investigating the relationship between the genetic mutation and the onset of scoliosis we have also investigated relationships with onset of epilepsy¹² and with behavioural abnormalities⁹. We found that children in whom we were not able to identify a *MECP2* mutation were more likely to have early onset of seizures. What we found with the behavioural abnormalities was that girls and young women with some of the milder mutations may be more capable of externalising and demonstrating some behaviours such as mood difficulties than those with more severe mutations. However, clinical severity may not necessarily reflect social severity in Rett syndrome. It is possible that for family and carers, caring for girls and young women in the milder group can at times be equally or more demanding than it is for the group with less functional ability.

We have carried out some studies where we have examined the effect of X inactivation. One study used information provided in the 2000 questionnaire and the calendars that were completed that year to look at the use of health services by girls and young women with Rett syndrome⁵. We found, as you might expect, that young girls used health services more and those with a milder clinical severity less. We also found that those who had random X inactivation (as opposed to skewed X inactivation) had greater health service use. This would imply that their clinical severity was greater which would be consistent with our thinking that skewed X inactivation provides some protection from the effects of the abnormality and those with random X inactivation do not have that protection. We have also carried out a study in association with the Institute of Medical Genetics at Cardiff University where we have been able to look at the effect of X inactivation on clinical severity in two particular mutations, the p.T158M and p.R168X mutations¹³. We demonstrated quite clearly for the first time that, for these two mutations, those whose X inactivation was skewed had a milder clinical picture than those in whom it was random.

Another genetic factor called X-chromosome inactivation may also affect clinical severity in Rett syndrome. In all female mammals, the cells contain two copies of the X chromosome, even though the information from only one copy is needed. Because of this, one of the X chromosomes in each cell must be "turned off" or inactivated. In most people, roughly half of their cells will have the X chromosome they inherited from their father active, and the other cells will have the X chromosome they inherited from their mother active. This is called "random X chromosome inactivation". In some of the girls with Rett Syndrome, however, their X inactivation is not random, and more than half of their cells show one (or the other) of their X chromosomes. This is known as skewed X inactivation. It is thought that if more than half of the cells of a girl with Rett syndrome showed the "bad copy" of *MECP2*, then they would have more severe symptoms, and conversely, if more than half of their cells show the "good copy", they would have milder symptoms.

Other interesting research we have carried out includes the diagnosis of Rett syndrome using DNA extracted from a baby tooth 14 years after the girl's death⁷. This was very important for the family who, during her lifetime, had never had a clear diagnosis for their daughter. Also we were able to describe the identification of a *MECP2* abnormality some time after the death of a baby boy who died at the age of 14 months¹⁰. He had developed severe neurological problems and breathing abnormalities in the early months of his life but during his lifetime no diagnosis for his condition was able to be made.

It is important that we raise awareness amongst clinicians not only about the presentation of *MECP2* abnormalities in baby boys but also about the variation in presentation of Rett syndrome in girls. We are extremely grateful to all the families in the Australian Rett Syndrome Study who have donated their time and energy to support this research which is leading the world in many areas.

Research at the NSW Centre for Rett Syndrome Research

It has also been a productive year for the research team in Sydney headed by Professor John Christodoulou, and they continue to move from strength to strength on several fronts. Screening of patients continues for genetic changes in the second Rett gene (*CDKL5*) which the Australian group discovered in a world first. The identification of individuals with genetic changes in *CDKL5* will allow doctors to be able to give more reliable genetic counselling.

Professor Christodoulou also continues to study where *CDKL5* acts in the cell, as this will give insights into how it can cause a clinical picture that overlaps with the problems caused by the original Rett gene (*MECP2*). To further help in these studies, it is important to have a laboratory mouse that is lacking the mouse equivalent of *CDKL5*, and to this end such an animal model is currently being created.

A *MECP2* mouse model has also been studied for the more common form of Rett syndrome, where the aim is to map the regions of the brain that are responsible for specific functional problems in the Rett mouse. This novel information may improve our understanding of brain function to a level that will allow us to consider how we could improve brain function in these regions.

Finally, a number of genes have been identified which seem to be under the specific control of *MECP2*, and which show altered activity in Rett syndrome. It is likely that these genes may directly contribute to the abnormalities in brain function seen in Rett syndrome, and with further study we are hopeful that this could give us an opportunity to design specific treatments for this currently incurable disorder.



International research

The Australian Rett syndrome team has actively sought engagement in international research. Since Rett syndrome is a rare disorder it is beneficial for researchers in different countries to work together to increase the power of their studies, share knowledge and experience and to prevent duplication of effort. Many previous Rett syndrome studies have only been carried out on a small number of cases which means that the results may not represent all the girls with Rett syndrome. As mentioned earlier by combining cases with other countries we have been able to improve our studies and obtain a better picture of the disorder. To foster this collaboration the Australian Rett syndrome team has developed close networks with overseas clinicians, geneticists and family support groups in Europe and America. These networks provide valuable support and advocacy for the InterRett project which collects information from families and clinicians all around the world.

In May 2006, Dr Leonard and Alison Anderson (who is the project coordinator of InterRett) attended an International Workshop to discuss clinical trials in Rett syndrome. Held in San Francisco, the workshop gave clinicians and geneticists from Europe, Asia and the USA the opportunity to exchange ideas and start the process of developing a framework to enable multi-centre clinical trials to test any future therapies or medical interventions that may become available.

Through our international initiatives we can further inform our important work here in Australian and maximise the use of information gained through the contributions of Australian families.

Scoliosis research

Scoliosis is one of the most common orthopaedic problems that develops in girls and young women with Rett syndrome and can significantly impact on their health and quality of life. We thought it would be helpful to families and health professionals if we were able to begin to find out whether some children with Rett syndrome are more or less likely to develop scoliosis.

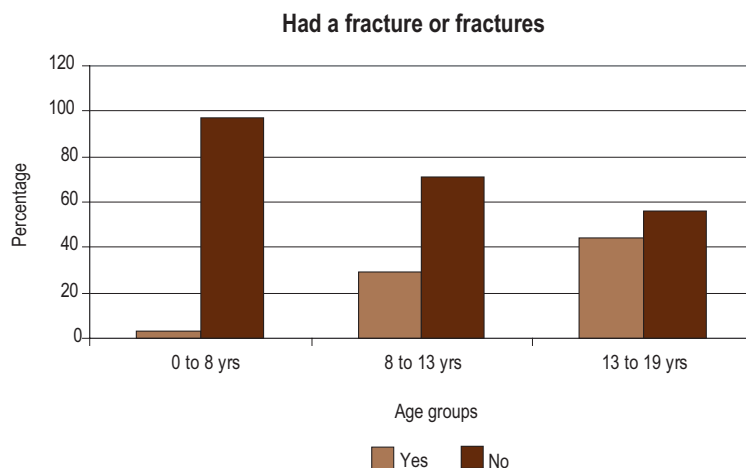
Recently completed research involved us using the data from questionnaires families completed on entry into the study and in the 2000 and 2002 period to investigate the development of scoliosis in girls with Rett syndrome. We found that the likelihood of scoliosis development increased with age: by 6 years of age 25% of girls had developed scoliosis rising to 75% by 13 years of age. The average age at onset for those who never walked was 7 years, much earlier than those girls who did walk (11.5 years). Overall, the average age for scoliosis onset was about 10 years. Children with signs of slow early development before 6 months, who were less mobile at ten months, and those who never walked were more likely to have an earlier onset of scoliosis¹¹.

The treatment of scoliosis currently involves the options of surgical procedures and more conservative management through postural inserts and braces. We are planning to undertake further research that looks at establishing some clinical guidelines for the management of scoliosis that will assist families and clinicians in making more informed choices as to the most suitable approach to use in managing scoliosis in Rett syndrome.

Densitometry study

One of the current research areas being focussed on by the Australian Rett Syndrome Study team is the measurement of bone density. By taking measurements from hand X rays we previously showed that osteopenia or thin bones is quite common in Rett syndrome and we also found that it can be associated with fractures.

Families' responses to the 'fractures' section in the 2004 questionnaire revealed that 28%, that is 55, of their daughters had had a fracture or fractures. As would be expected, the proportion of families reporting their daughter had had a fracture during the course of their life increased for each developmental age group. Only a few families with daughters who are now young women answered this question so they were not included in comparisons between age groups. At the time of completing the questionnaire, twenty per cent of girls and young women with Rett syndrome had already been diagnosed with osteoporosis.



Families whose daughter had had a fracture were asked if there were any problems related to the fracture or healing. While most families reported there were *'no problems with healing.... healed in expected time frame'*, some families reported significant problems following the fracture.

'Yes...took longer to heal than with a usual broken arm...her arm never knitted straight'

'Not enough bone density to operate...bone impacted on itself about ¼ inch so left leg is now shorter'

'Refused to use right arm (fractured wrist) for few months and had to put bells on her wrist to remind her it was there to use....stopped holding drinking cup from this time and feeding herself aided with a spoon'

The densitometry study focuses on measuring bone density in Australian girls and young women with Rett syndrome. It aims to identify those factors that are associated with decreased bone density and strength and those that protect against it. In order to obtain the best results for the study, we are trying to ensure that the majority of bone densitometry assessments are carried out at centres that use the same or similar equipment.

Where possible, families are being asked to have testing done at one of these centres across the country: Children's Hospital in Westmead, Sydney; Monash Medical Centre in Melbourne; the Royal Children's Hospital in Brisbane; Benson's Radiology in Adelaide and the Perth Radiological Clinic in Perth.

We thank families for their ongoing participation in this important work and look forward to being able to begin to report some meaningful results over the coming year.

Epilepsy study

As most of you will be aware we are continuing our research into epilepsy in girls and young women with Rett syndrome. Recently completed research used the data supplied by families on enrolment to the study and data from the 2000, 2002 and 2004 questionnaires to try to understand what some of the predictors of seizure onset may be in girls and young women with Rett syndrome. In this study we found that seizures were reported in about 80% of girls with Rett syndrome. The average age for the onset of seizures was four years, with 25% of children having seizures by the age of two years, 50% by the age of four years and 78% by the age of ten years. For children who don't develop the ability to walk, the risk of seizures is significantly increased.

Epilepsy can be one of the most challenging medical problems associated with the Rett syndrome disability and can place significant additional stress on families. While our work to date has told us about when girls with Rett syndrome develop seizures and which girls may be more at risk to do so than others, we know little about the nature and type of seizures that occur. About quarter of families answering the 2004 questionnaire indicated their daughter was having significant current problems due to their seizure activity.

'Usually sleeps after a seizure...sometimes vomits while in or just after a big seizure... sometimes injures herself, usually feet and legs'

'Our daughter is experiencing increased seizure activity presently. The seizure types are myoclonic, several drop attacks a day....can be in clusters or single events.....the past month has been a very unstable period'

'She bites her tongue or lip very badly...this has been happening in the last couple of years and causes huge problems with feeding'

'It is under control at present, but affects her everyday life in that she is lethargic and uninterested in anything when having problems with seizures'

In the coming few months we will be telephoning families whom we know has a daughter with epilepsy to obtain information that may help us understand more about the nature and burden of this condition.

The video study

The video assessment is one of the methods that has been developed recently for additional description of girls with Rett syndrome. The idea originated from families who from time to time provided video material to us to supplement their questionnaire data. We considered this to be a valuable resource and subsequently videotaped two children (9 and 11 years) with Rett syndrome to record mobility, communication skills and other functional abilities during activities of daily living. These initial videos all helped to stimulate the development of the video assessment.

We envisage many potential benefits from use of video assessment in girls and young women with Rett syndrome. A home-filmed video allows us to:

- Gain additional perspectives on abilities and behaviours including the demonstration of greater detail of abilities.
- Observe subtle yet significant changes that can occur and are perceived by family members but which are difficult to measure on some other assessments.
- Observe improved demonstration of abilities because filming takes place in a familiar as opposed to a less familiar clinical setting.
- Observe interaction with family members and friends.
- Obtain a permanent visual record which is available for later comparisons.
- Receive information from those who live in a diversity of locations, including rural and remote communities.



The video assessment has two sections – a written questionnaire checklist and a guide for filming together with a demonstration video. Parents complete the checklist, which collects useful information based on their bank of knowledge of their child’s function and behaviours.

The written checklist (called the Functional Ability Checklist) collects information about the activities to be filmed including eating and drinking, communication, hand function, dressing and personal care, and posture and mobility.

The filming protocol and demonstration video guide the filming of a set of activities and allow for systematic observation by the researchers of the function in Rett syndrome.

We have now received over a hundred videos from families. They show a wide range of abilities in girls and young women with ages ranging from one to 27 years.

We are currently analysing the parts of the video that show mobility skills such as sitting, transferring, standing and walking.

- Many girls could sit on the floor (75%), a chair (64%) or a stool (71%) without needing assistance.
- A little less than half of the girls (43%) were able to walk independently and could also side step and turn 180 degrees whilst walking, strategies that help to negotiate the way through the environment when walking.
- A smaller percentage of the girls could stand with no assistance for 3 seconds (39%), 10 seconds (34%) and 20 seconds (23%), and many of the girls could stand when given assistance. Approximately one third of girls could not stand.
- The percentage of girls who could transfer without assistance was smaller than the percentage who could sit, walk or stand. For example, 21% could get up to standing from sitting in a chair, 14% could bend and touch the floor then return to standing, and 9% could stand up from sitting on the floor without assistance.
- A small proportion of girls (14%) were able to run.



Only the skills of sitting on the floor and getting up from the floor into the standing position without assistance were more likely to be demonstrated by younger girls than older girls and women with Rett syndrome. Otherwise, we saw no relationship between age and the level of assistance for any of the other mobility skills. This information suggests that aiming to maintain mobility skills is an important objective for girls with Rett syndrome.

Currently, we are conducting additional analyses of the mobility information and are also coding other skills, such as feeding and hand function, contained in the videos. Additional participation from families who would like to provide a video using this assessment is always welcomed.

The Australian Rett Syndrome Study continues striving to achieve its aim of understanding the disability of Rett syndrome. As part of this process, the team recently formed a Consumer Reference Group to ensure family representation and input into issues relating to the design, management and output of the study particularly relating to communication and feedback to families. To date, the group has met on four occasions, the first meeting being held in August 2005. The group is made up of 11 families, representing all States of Australia except the Northern Territory and Tasmania.

Ongoing areas of focus for the Australian Rett Syndrome Study team for the 2006/2007 period include:

- Determining health-associated costs; education-associated costs and costs to the family associated with Rett syndrome.
- Continuing the telephone interviews to help determine classification of seizure type and to commence the analysis of Electroencephalograph (EEG) records.
- Describing the patterns of feeding and growth of children with Rett syndrome.
- Examining the patterns of sleep problems in children with Rett syndrome and the factors associated with these.
- Describing the nature and burden of epilepsy in Rett syndrome.
- Describing gross motor and other areas of functioning in Rett syndrome through use of video footage.

References

- ¹ Colvin, L., S. Fyfe, et al. (2003). Describing the phenotype in Rett syndrome using a population database. *Archives of Diseases in Childhood* 88(1): 38-43.
- ² Leonard, H., L. Colvin, et al. (2003). Patients with the R133C mutation: is their phenotype different from patients with Rett syndrome with other mutations? *Journal of Medical Genetics* 40(5): e52.
- ³ Colvin, L., H. Leonard, et al. (2004). Refining the phenotype of common mutations in Rett syndrome. *Journal of Medical Genetics* 41(1): 25-30.
- ⁴ Leonard, H., H. Moore, et al. (2005). Genotype and early development in Rett syndrome: The value of international data. *Brain and Development* 27 (Suppl 1): S59-68.
- ⁵ Moore, H., H. Leonard, et al. (2005). Health service use in Rett syndrome. *Journal of Child Neurology* 20(1): 42-50.
- ⁶ Jian, L., H. L. Archer, et al. (2005). p.R270X MECP2 mutation and mortality in Rett syndrome. *European Journal of Human Genetics*.
- ⁷ Leonard, H. D., M. Turbett, et al. (2005). Effectiveness of posthumous molecular diagnosis from a kept baby tooth. *Lancet* 366.
- ⁸ Laurvick, C. L., N. de Klerk, et al. (2006). Rett syndrome in Australia: a review of the epidemiology. *Journal of Pediatrics* 148 (3): 347-52.
- ⁹ Robertson, L., S. Hall, et al. (2006). The association between behaviour and genotype in Rett Syndrome using the Australian Rett Syndrome Database. *American Journal of Medical Genetics- Part B Neuropsychiatrics* 141(2): 177-83.
- ¹⁰ Kankirawatana, P., H. Leonard, et al. (2006). Early progressive encephalopathy in males and MECP2 mutations. *Neurology* 67: 164-166.
- ¹¹ Ager, S., S. Fyfe, et al. (in press). Predictors of scoliosis in Rett syndrome. *Journal of Child Neurology*.
- ¹² Jian, L., L. Nagarajan et al. (in press). Predictors of seizure onset in Rett syndrome. *Journal of Pediatrics*.
- ¹³ Archer, H. J., Evans, J et al. (in press) Correlation between proportion of active mutated allele and clinical severity in Rett syndrome patients with a p.R168X or p.T158M MECP2 mutation. *Journal of Medical Genetics*.

Publications

In press

Ager, S., S. Fyfe, et al. (in press). Predictors of scoliosis in Rett syndrome. *Journal of Child Neurology*.

Laurvick, C; Msall, M; Silburn, S; Bower, C; de Klerk, N; Leonard, H. (in press). Physical and mental health in mothers caring for a child with Rett syndrome. *Pediatrics*.

Jian, L; Nagarajan, L; de Klerk, N; Ravine, D; Bower, C; Anderson, A; Williamson, S; Christodoulou, J; Leonard, H. (in press). Predictors of seizure onset in Rett syndrome. *Journal of Pediatrics*.

Archer, H. J., Evans, J et al. (in press) Correlation between proportion of active mutated allele and clinical severity in Rett syndrome patients with a p.R168X or p.T158M MECP2 mutation. *Journal of Medical Genetics*.

2006

Archer, H., J. Evans, et al. (2006). NTNG mutations are a rare cause of Rett syndrome. *American Journal of Medical Genetics Part A* 140A (7): 691-694.

Kankirawatana, P., H. Leonard, et al. (2006). Early progressive encephalopathy in males and MECP2 mutations. *Neurology* 67: 164-166.

Laurvick, C. L., N. de Klerk, et al. (2006). Rett syndrome in Australia: a review of the epidemiology. *Journal of Pediatrics* 148 (3): 347-52.

Robertson, L., S. Hall, et al. (2006). The association between behaviour and genotype in Rett Syndrome using the Australian Rett Syndrome Database. *American Journal of Medical Genetics-Part B Neuropsychiatrics* 141(2): 177-83.

2005

Jian, L., H. L. Archer, et al. (2005). The p.R270X MECP2 mutation and mortality in Rett syndrome. *European Journal of Human Genetics*.

Leonard, H., H. Moore, et al. (2005). Genotype and early development in Rett syndrome: The value of international data. *Brain and Development* 27 (Suppl 1): S59-68.

Leonard, H. D., M. Turbett, G. R. Laing, N.G. Bower, C. Ravine, D. (2005). Effectiveness of posthumous molecular diagnosis from a kept baby tooth. *Lancet* 366.

Moore, H., H. Leonard, et al. (2005). Health service use in Rett syndrome. *Journal of Child Neurology* 20(1): 42-50.

Moore, H., H. Leonard, et al. (2005). InterRett: The application of bioinformatics to International Rett syndrome research. *Annals of Human Biology* 32(2): 228-36.

2004

Colvin, L., H. Leonard, et al. (2004). Refining the phenotype of common mutations in Rett syndrome. *Journal of Medical Genetics* 41(1): 25-30.

Leonard, H., L. Slack-Smith, et al. (2004). How can the Internet help parents of children with rare neurologic disorders? *Journal of Child Neurology* 19(11): 902-7.

Leonard, H., L. Weaving, et al. (2004). Trisomy 21 and Rett syndrome: a double burden. *Journal of Paediatrics and Child Health* 40(7): 406-9.

Moore, H., N. Leonard, et al. (2004). Longitudinal data collection using the Internet: a novel approach for adolescents. *Australasian Epidemiologist* 11(1): 20-24.

Weaving, L. S., J. Christodoulou, et al. (2004). Mutations of CDKL5 cause a severe neurodevelopmental disorder with infantile spasms and mental retardation. *American Journal of Human Genetics* 75(6): 1079-93.

2003

Colvin, L., S. Fyfe, et al. (2003). Describing the phenotype in Rett syndrome using a population database. *Archives of Diseases in Childhood* 88(1): 38-43.

Fyfe, S., A. Cream, et al. (2003). InterRett and RettBASE: International Rett Syndrome Association databases for Rett syndrome. *Journal of Child Neurology* 18(10): 709-13.

Gill, H., J. P. Cheadle, et al. (2003). Mutation analysis in the MECP2 gene and genetic counselling for Rett syndrome. *Journal of Medical Genetics* 40(5): 380-4.

Leonard, H., L. Colvin, et al. (2003). Patients with the R133C mutation: is their phenotype different from patients with Rett syndrome with other mutations? *Journal Medical Genetics* 40(5): e52.

Umansky, R., J. S. Watson, et al. (2003). Hand preference, extent of laterality, and functional hand use in Rett syndrome. *Journal of Child Neurology* 18(7): 481-7.

Weaving, L. S., S. L. Williamson, et al. (2003). Effects of MECP2 mutation type, location and X-inactivation in modulating Rett syndrome phenotype. *American Journal of Medical Genetics A* 118(2): 103-14.

2001

Ellaway C, Badawi N, Raffaele L, Christodoulou J, and Leonard H. (2001). A case of multiple congenital anomalies in association with Rett syndrome confirmed by MeCP2 mutation screening. *Clinical Dysmorphology* 10(3): 185-8.

Ellaway C, Peat J, Leonard H, Christodoulou J. (2001). Sleep dysfunction in Rett syndrome. *Brain & Development* 23 (Suppl 1): S85-S89.

Ellaway C, Peat J, Williams K, Leonard H, Christodoulou J. (2001). Long term open label trial of L-Carnitine in Rett syndrome. *Brain & Development* 23 (Suppl 1): S85-S89.

Fyfe S, Leonard H, Gelmi R, Tassell A and Strack R. (2001). Using the internet to pilot a questionnaire on childhood disability in Rett syndrome. *Child: Care, Health and Development* 27(6):535-543.

Kerr AM, Nomura Y, Armstrong D, Anvret M, Belichenko PV, Budden S, Cass H, Christodoulou J, Clarke A, Ellaway C, d'Esposito M, Francke U, Hulten M, Julu P, Leonard H, Naidu S, Schanen C, Webb T, Witt Engerstrom I, Yamashita Y, Segawa M. (2001). Guidelines for the reporting of clinical features in cases with MECP2 mutations. *Brain & Development* 23: 208-211.

Leonard H, Fyfe S, Leonard S, Msall M. (2001). Functional status, medical impairments, and rehabilitation resources in 84 subjects with Rett syndrome: a snapshot across the world from the parental perspective. *Disability and Rehabilitation* 23 (3,4):107-117.

Leonard H, Silberstein J, Falk R, Houwink-Manville I, Ellaway C, Raffaele L, Witt Engerstrom I, Schanen C. (2001). Occurrence of Rett syndrome in males. *Journal of Child Neurology* 16(5): 333-8.

2000

Cheadle JP, Gill H, Fleming N, Maynard J, Kerr A, Leonard H, Krawczak M, Cooper DN, Lynch S, Thomas N, Hughes H, Hulten M, Ravine D, Sampson JR, Clarke A. (2000). Long-read sequence analysis of the MECP2 gene in Rett syndrome patients: correlation of disease severity with mutation type and location. *Human Molecular Genetics* 9(7):1119-1129.

Leonard H, Fyfe S, Dye D, Hockey A, Christodoulou J. (2000). Family data in Rett syndrome: association with other genetic disorders. *Journal of Paediatrics and Child Health* 36(4):336-339.

Leonard H, Fyfe S, Dye D, Leonard S. (2000). Using genetic epidemiology to study Rett syndrome: the design of a case control study. *Paediatric and Perinatal Epidemiology* 14 (1):85-95.

1999

Ellaway CJ, Sholler G, Leonard H, Christodoulou J. (1999). Prolonged QT interval in Rett syndrome. *Archives of Diseases in Childhood* 80(5):470-472.

Ellaway C, Williams K, Leonard H, Higgins G, Wilcken B, Christodoulou J. (1999). Rett Syndrome: Randomised Controlled Trial of L-carnitine. *Journal of Child Neurology* 14(3): 162-167.

Fyfe S, Leonard H, Dye D, Leonard S. (1999). Patterns of pregnancy loss, perinatal mortality and postneonatal childhood deaths in families of a girl with Rett syndrome. *Journal of Child Neurology* 14(7):440-445.

Leonard H, Fyfe S, Dye D, Leonard S. (1999). Familial aggregation in Rett syndrome: What is the evidence for clustering of other disorders in the extended families of affected girls? *American Journal of Medical Genetics* 82(3): 228-234.

Leonard H, Glasson E, Thomson M, Fyfe S, Christodoulou J, Ellaway C, Leonard S, Bower C. (1999). Metacarpophalangeal pattern profile and bone age in Rett syndrome: Further radiological clues to the diagnosis. *American Journal of Medical Genetics* 83(2): 88-95.

Leonard H, Thomson R, Glasson E, Fyfe S, Leonard S, Bower C, Christodoulou J, Ellaway C. (1999). A population based approach to the investigation of osteopenia in Rett syndrome. *Developmental Medicine and Child Neurology* 41(5):323-8.

1998

Ellaway C, Buchholz T, Smith A, Leonard H, Christodoulou J. (1998). Rett syndrome: Significant clinical overlap with Angelman syndrome but not with methylation status. *Journal of Child Neurology* 13(9): 448-451.

Glasson EJ, Thomson MR, Fyfe S, Leonard S, Bower C, Rousham E, Christodoulou J, Ellaway C, Leonard H. (1998). Diagnosis of Rett syndrome: Can a simple radiograph help? *Developmental Medicine and Child Neurology* 40: 737-742.

Leonard H, and Bower C. (1998). Is the girl with Rett syndrome normal at birth? *Developmental Medicine and Child Neurology* 40(2): 115-121.

1997

Leonard H. (1993). Rett syndrome: opportunity for Australian study (letter). *Medical Journal of Australia* 159(11/12): 832.

Leonard H, Bower C, and English D. (1997). The prevalence and incidence of Rett syndrome in Australia. *European Child & Adolescent Psychiatry* 6 (Suppl.1): 8-10.

Leonard H, Thomson R, Bower C, Fyfe S, and Constantinou J. (1995). Skeletal abnormalities in Rett syndrome: Increasing evidence for dysmorphogenetic defects. *American Journal of Medical Genetics* 58(3): 282-285.

Reports, books & theses

Leonard, H., Ravine, D., Rett syndrome. *Management Guidelines: People with Developmental and Intellectual Disabilities*. (Second Edition) Therapeutic Guidelines Limited, 2005. p. 277-80.

Leonard, H. and S. Leonard (2003). The ICF and Rett Syndrome. ICF Australian User Guide. Version 1.0. Disability Series. Canberra, Australian Institute of Health and Welfare: 99-105.

Leonard, S. (2002). The Australian Rett Syndrome Study Inaugural Report. Perth, Telethon Institute for Child Health Research: 1-42.

Leonard H, Fyfe S, Ellaway C. Possible link between skeletal and electrocardiographic abnormalities and autonomic dysfunction in Rett syndrome. In: *Rett Disorder and the developing brain* (Kerr & Witt-Engerstrom) Oxford University Press. Oxford 2000.

Alessandri L, Leonard H, Blum L, and Bower C. (1997). *Disability Counts: A profile of people with disability in Western Australia*. Perth, Western Australia: Disability Services Commission, 1996.

Leonard H. (1996). Rett syndrome in Australia. Department of Public Health, University of Western Australia.

Leonard H. The genetics of Rett syndrome. *Bulletin Human Genetics Society of Australia* 1994; 7 (1): 18-20.

Presentations

2006

"InterRett" Scottish Rett Syndrome Association. Glasgow, Scotland.

"InterRett and the natural history of Rett syndrome", National Institute for Health/International Rett Syndrome Association. San Francisco, USA.

"The impact of having a sibling with a developmental disability: parental perspectives in two disorders". Telethon Institute for Child Health Research Away Days. Perth, Australia.

2005

"InterRett. Rett syndrome update for Parents", Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead. Sydney, Australia.

"Measuring the well-being of families with Rett syndrome child. Rett syndrome update for Health Professionals", Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead. Sydney, Australia.

"Clinical variability and genotype/phenotype variability. Rett syndrome update for Health Professionals", Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead. Sydney, Australia.

"AussieRett study and Epidemiology. Rett syndrome update for Parents", Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead. Sydney, Australia.

"AussieRett and InterRett studies. Rett syndrome update for Health Professionals", Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead. Sydney, Australia.

"The experience of mealtimes in girls with Rett Syndrome", Rett Syndrome Workshop for Parents, Australian Paediatric Surveillance Unit, The Children's Hospital at Westmead. Sydney, Australia.

"The p.R270X MECP2 mutation and mortality in Rett syndrome", Annual Conference of the Human Genetics Society of Australasia. Newcastle, Australia.

"Demonstrating the use of video analysis in the investigation of behavioural phenotype; an example from Rett syndrome", 9th International Symposium: Treatment of Behavioural Problems in Neurodevelopmental Disorders, Society for the Study of Behavioural Phenotypes. Cairns, Australia.

2004

"Rett syndrome research in Australia - past, present and future", Hospital Sant Joan de Déu. Barcelona, Spain.

"InterRett IRSA Rett Phenotype Database", Future Horizons Rett Syndrome Conference. Ottawa, Canada.

"Rett syndrome research in Australia-past, present and future", Child Neurology Study Group. Margaret River, Australia.

"InterRett: International developments in Rett syndrome research", Annual Scientific Meeting of the Royal Australian College of Physicians. Canberra, Australia.

Genotype and early development in Rett syndrome: The value of international data. Human Genetics Society of Australasia WA Branch meeting. Perth, Australia.

2003

"Rett syndrome: Surveillance and beyond", Australian Paediatric Surveillance Unit Annual Scientific Meeting. Hobart, Australia.

"Rett syndrome", Neurosciences Initiative Workshop. Institute for Child Health Research. Perth, Australia.

2002

"Rett syndrome: evolution from genotype to phenotype", Annual Conference of the Human Genetics Society of Australasia. Adelaide, Australia.

"Now that the gene has been found: describing the phenotype in Rett syndrome using a national database", Joint Congress of International Child Neurology Association and Asian and Oceanic Child Neurology Association. Beijing, China.

"Now that the gene has been found: describing the phenotype in Rett syndrome using a national database", Rett Syndrome Research Foundation Conference. Baltimore, USA.

"The evolution of Rett syndrome from phenotype to genotype", Annual Conference of Human Genetics Association of Australasia. Adelaide, Australia.

"The evolution of Rett syndrome from phenotype to genotype", Grand Round, Princess Margaret Hospital. Perth, Australia.

2001

Dr H Leonard invited as a member of a clinical consensus panel, to review clinical criteria for Rett syndrome and to consider severity scales for Rett syndrome, Baden Baden, Germany.

"Epidemiological update of Rett syndrome following recent genetic advances", Telethon Institute for Child Health Research Away Days. Perth, Australia.

"Trisomy 21 and Rett syndrome: a double burden", Annual Conference of the Human Genetics Association of Australasia. Cairns, Australia.

"Trisomy 21 and Rett syndrome: a double burden", Human Genetics Society of Australasia WA Branch meeting. Perth, Australia.

"Rett syndrome in Australia from the nineties to the new millennium", Grand Round, Women and Children's Hospital. Adelaide, Australia.

"Beyond classical Rett syndrome: exploring the MECP2 phenotype", Child Neurology Study Group. Clare Valley, Australia.

"Rett Syndrome in the new millennium", Conference of the National Association of Neurophysiology Technicians. Perth, Australia

2000

"Exploring the male phenotype", World Conference on Rett Syndrome. Nagano, Japan.

"Rett syndrome in Australia: seven years on", World Conference on Rett Syndrome. Nagano, Japan.

"Does Rett syndrome occur in males?", Annual Conference of the Human Genetics Association of Australasia. Sydney, Australia.

"A Diagnosis of Rett Syndrome: What Does the Future Hold for the Child and Her Family?", Telethon Institute for Child Health Research Away Days. Perth, Australia.

"Measuring the burden of disability in Rett syndrome: preliminary findings using two different approaches", Research and Advances Seminar, Princess Margaret Hospital. Perth, Australia.

"Rett syndrome in Australia: seven years on", Annual Human Genetics Society of Australasia WA Branch meeting. Perth, Australia.

1999

"Rett syndrome: APSU and beyond", Annual Scientific Meeting of the Royal Australian College of Physicians. Perth, Australia.

1998

"Bone quality and its effects in Rett syndrome", Folke Bernadotte International Memorial Conference. Stockholm, Sweden.

"Perinatal and infant deaths in families of girls with Rett syndrome", Australian and New Zealand Perinatal Society Conference. Alice Springs, Australia.

1997

"Osteopenia in Rett syndrome", Annual Conference of the Australian and New Zealand College of Paediatrics. Christchurch, New Zealand.

"Rett Syndrome", Conference of the National Association of Neurophysiology Technicians. Perth, Australia.

"An investigation of familial co-aggregation of other conditions with Rett syndrome", Annual Conference of the Human Genetics Association of Australasia 'Human Genetics: Diversity and Disease'. Fremantle, Australia.

"The Hands and Feet in Rett syndrome", Annual Conference of the Human Genetics Association of Australasia 'Human Genetics: Diversity and Disease'. Fremantle, Australia.

"Radiological clues to the neuroendocrine basis of Rett syndrome", Annual Conference of the Human Genetics Association of Australasia 'Human Genetics: Diversity and Disease'. Fremantle, Australia.

"Lightning strikes twice - a family with Rett syndrome in two generations", Annual Conference of the Human Genetics Association of Australasia 'Human Genetics: Diversity and Disease'. Fremantle, Australia.

"A boy with Rett-like features", Annual Conference of the Human Genetics Association of Australasia 'Human Genetics: Diversity and Disease'. Fremantle, Australia.

"Carnitine: Double blinded crossover trial in 35 females with Rett syndrome", Annual Conference of the Human Genetics Association of Australasia 'Human Genetics: Diversity and Disease'. Fremantle, Australia.

"Rett Syndrome", Forum on Behavioural Stereotypes in Intellectual Disability, Monash Medical Centre. Melbourne, Australia.

1996

"Ascertainment of a rare childhood condition in Australia", Annual Conference of the Public Health Association of Australia Inc., Perth, Australia.

"Families living with Rett syndrome: their needs and social support networks", World Congress on Rett Syndrome. Gothenburg, Sweden.

"Rett syndrome in Australia: Epidemiological data - distribution of classical and atypical females", World Congress on Rett Syndrome, Gothenburg, Sweden.

"A case of variant Rett syndrome with unusual neuropathological findings", World Congress on Rett Syndrome, Gothenburg, Sweden.

"Further documentation of familial Rett syndrome", World Congress on Rett Syndrome, Gothenburg, Sweden.

1995

"Focussing in on the genome through the hands and feet in Rett syndrome", Annual Conference of the Australian and New Zealand College of Paediatrics. Adelaide, Australia.

1994

"Solving the puzzle of Rett syndrome", National Conference of the Australian Society for the Study of Intellectual Disability, Perth, Australia.

"Rett syndrome: Care and support of the child and family in Australia", National conference of the Australian Society for the Study of Intellectual Disability, Perth, Australia.

"Skeletal abnormalities in Rett syndrome: Have we found a dysmorphic marker?", The 8th Annual Scientific Conference of The Australasian Society for Human Biology, Perth, Australia.

"The First Year of the APSU: The perspective of the investigators of Rett syndrome", Research and Advances Seminar, Princess Margaret Hospital, Perth, Australia.

1993

"Rett syndrome: Gene to Gesture", Forum on Learning Disability, Royal Society of Medicine, London, UK.

"Rett syndrome in Australia", Australian Society for the Study of Intellectual Disability. Newcastle, Australia.

"Rett syndrome in Australia", Annual scientific meeting of Australian College of Paediatrics and the Paediatric Research Society of Australia. Melbourne, Australia.

Study personnel, students and collaborators in 2006

Telethon Institute for Child Health Research

Head: Clinical Associate Professor Helen Leonard
Professor Carol Bower
Professor Nicholas de Klerk
Professor Sven Silburn
Mrs Carol Philippe
Mrs Alison Anderson
Ms Orla McIlroy
Mrs Anne Pugh
Dr Le Jian
Dr Jenny Downs
Ms Ami Bebbington
Ms Paula Dyke

Dr Deidra Young
Ms Karina Aiberti
Ms Heather Monteiro
Dr Wendy Oddy
Mr Peter Jacoby
Mrs Kathryn Webb
Dr Seonaid Mulroy
Dr Alpana Kulkarni
Ms Laila Robertson (previous student)
Ms Sarah Ager (previous student)
Ms Crystal Laurvick (previous staff)
Ms Hannah Moore (previous staff)

Princess Margaret Hospital for Children

Dr Lakshmi Nagarajan
Dr Jackie Scurlock
Dr Cathy Kiraly-Borri

Curtin University of Technology

Professor Susan Fyfe
Ms Amanda Jefferson
Ms Anke Bergmann
Ms Joanna Lister (previous student)

University of Western Australia

Ms Delia Hendrie
Dr Sonj E Hall (previous staff member)
Professor Linc Schmidt

Royal Perth Hospital & West Australian Institute of Medical Research & Centre for Medical Research, University of Western Australia

Professor David Ravine
Professor Nigel Laing
Dr Mark Davis
Dr Alka Saxena
Dr Vicki Fabian
Ms Danielle Delagarde

NATIONAL

Children's Hospital at Westmead, Sydney

Professor John Christodoulou
Dr Carolyn Ellaway
Dr Bruce Bennetts
Ms Sarah Williamson
Ms Rose White
Dr Albert Mansour
Ms Julie Briody
Ms Sue Thompson

Monash Medical Centre

Associate Professor Boyd Strauss

Sydney Children's Hospital

Dr Helen Woodhead

Royal Children's Hospital Melbourne

Professor Sheena Reilly
Dr Gordon Baikie

Women's and Children's Hospital, Adelaide

Dr Elizabeth Thompson

INTERNATIONAL

**University of Chicago Pritzker School of
Medicine, Kennedy Mental Retardation Section of
Developmental and Behavioral Pediatrics, Comer
Children's and LaRabida Children's Hospitals,
Chicago, Illinois, USA**

Professor Michael Msall

**Center for Genetic Disorders of Cognition and
Behavior, Kennedy Krieger Institute and Johns
Hopkins University School of Medicine, Maryland,
USA**

Dr Walter Kaufmann

Cardiff University, Wales

Professor Angus Clarke
Dr Hayley Archer

University of Alabama at Birmingham, USA

Professor Alan Percy

University of Glasgow, Scotland

Dr Alison Kerr
Dr Bronwen Burford
Dr Mark Bailey

Hospital Sant Joan de Déu, Barcelona, Spain

Dr Merce Pineda

Hopital Necker Enfants Malades, Paris, France

Dr Nadia Bahi-Buisson

Victoria General Hospital, Victoria, BC, Canada

Dr Patrick McLeod

Peking University First Hospital, Beijing, China

Professor Wu

Sheba Medical Center, Ramat-Gan, Israel

Dr Bruria Ben-Zeev

Acknowledgements

We would like to acknowledge the funders of our Australian Rett syndrome researchers as well as those who have contributed specifically to the publication of this report as well as to the promotion of the research in other ways.

Funding of the current Australian Rett Syndrome research program is provided by the National Institutes of Health (1 R01 HD43100-01A1) and the National Medical and Health Research Council (NHMRC) under project grant 303189. We'd also like to acknowledge the funding contributions provided by the Rett Syndrome Australian Research Fund over the last ten years.

We would like to express our gratitude to all the families and clinicians who have contributed to the study in an ongoing way; the Australian Paediatric Surveillance Unit (APSU) and the Rett Syndrome Association of Australia which facilitated case ascertainment in Australia.

Without the families this report would not have been possible and we'd also like to thank families particularly for providing the photographs which have been used throughout the report.

Finally we would also like to express our appreciation of the specific contributions made for the funding of this report by the following organisations:

Rett Syndrome Association of Australia

Rett Syndrome Australian Research Fund

The Australian Rett Syndrome Study

Telethon Institute for Child Health Research

100 Roberts Road, Subiaco
Western Australia 6008

t 61 8 9489 7790

f 61 8 9489 7700

e rett@ichr.uwa.edu.au

w <http://www.ichr.uwa.edu.au/rett/aussierett>

