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ORIGINAL PAPER

Psychological Well-Being of Mothers and Siblings in Families of Girls and Women with Rett Syndrome

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Abstract Few published studies have reported on the psychological well-being of family members of individuals with Rett syndrome (RTT). Eighty-seven mothers of girls and women with RTT completed a questionnaire survey about their daughters' behavioral phenotype, current health, and behavior problems, and their own and a sibling's well-being. Mothers reported increased anxiety but similar levels of depression when compared to a normative sample. Across all problem domains on the Strengths and Difficulties Questionnaire, child and adolescent siblings (n = 39) were reported by mothers to have fewer difficulties than a normative sample. The severity of their daughters' RTT behavioral phenotype predicted increased anxiety and stress for mothers. Increased RTT daughters' current health problems predicted more maternal perceptions of positive gain.

Keywords Rett syndrome · Siblings · Mothers · Maternal depression · Strengths and Difficulties Questionnaire · Families

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Introduction

Rett syndrome (RTT) is a genetic disorder that causes severe cognitive and physical impairments. In its classic form, it appears to affect almost exclusively females, with an incidence of up to one in every 10,000 live female births. The cause of RTT is most often a mutation in the methyl-CpG binding protein-2 (*MECP2*) gene, located on the X chromosome at *Xq28* (Amir et al. 1999). Although a *MECP2* mutation is found in most cases of the classic form, RTT remains a clinical rather than a molecular diagnosis. According to the current RTT diagnostic criteria (Neul et al. 2010), classic RTT requires apparently normal psychomotor development in the first 6 months of life followed by a period of regression, which is not due to brain injury secondary to trauma, neurometabolic disease, or severe infection, and involves partial or complete loss of acquired purposeful hand skills and language, gait abnormalities and the development of stereotypic hand movements, followed by stabilization or even some degree of recovery. An important aspect of the regression is a period of social withdrawal or impaired communication. Atypical RTT requires a similar period of regression and subsequent stabilization/recovery, at least two of the above four behavioral manifestations and the presence of at least five (out of 11) supportive criteria. Other variant forms have also been described (Neul et al. 2010).

Given the severe to profound intellectual disability present in RTT, and following a family systems perspective (Cridland et al. 2014; Hastings et al. 2014; Seligman and Darling 2009), it is important to examine the putative impact of raising an individual with RTT on family members. In population-defined samples less open to typical methodological biases, mothers of children with general developmental disability report increased stress and mental

health problems (Emerson et al. 2006; Totsika et al. 2011a, b) compared to mothers of children without developmental disability. Siblings of children with disabilities may also have higher levels of psychological problems compared with children who have no siblings with disabilities but these differences tend to be small in terms of effect size (Goudie et al. 2013; Neely-Barnes and Graff 2011).

Despite the significant care needs associated with Rett syndrome, there has been little research designed to understand the experiences of families of girls and women with the syndrome. Using normative comparisons, two studies found increased parenting stress in samples of parents of individuals with Rett syndrome (Byiers et al. 2014; Perry et al. 1992). Also using normative data and a population Rett syndrome sample in Australia, Laurvick et al. (2006) and Urbanowicz et al. (2011) showed that maternal mental health was poorer but maternal physical health differed little from norms. In terms of explaining some of the variability in parental stress, there has been little consistency in the factors examined with correlates identified including the following: various dimensions of the Rett syndrome behavioral phenotype (Laurvick et al. 2006), the cost of specialist equipment and use of respite care (Urbanowicz et al. 2011), and comorbid epilepsy and parental perceptions that the individual with Rett syndrome may be experiencing pain (Byiers et al. 2014).

Two qualitative studies have also examined family experiences. Lim et al. (2013) interviewed 14 mothers of individuals with Rett syndrome in China and found that families had significant needs for support with their relative's health problems. In a survey study, Mulroy et al. (2008) asked parents of individuals with Rett or Down syndromes about sibling experiences in the families. Parents were slightly more likely to report beneficial outcomes for siblings of individuals with Down syndrome (80 vs. 71 % for Rett syndrome), and less likely to report disadvantageous outcomes (75 vs. 83 % for Rett syndrome). Mulroy et al. (2008) also reported qualitative comments from parents who were concerned about the impact of a range of experiences on siblings especially in Rett syndrome families, including restricted family time (partly due to lengthy hospital visits by the individual with Rett syndrome), and restricted opportunities for the family to socialize with others.

Given the small number of family studies focused on Rett syndrome, there is clearly a need for more research. In addition, there is a need to locate family research on this syndrome within the broader developmental disabilities family research field. Thus, there is still a need to understand whether family members of individuals with Rett syndrome may be a high risk group for stress and other psychological outcomes. In addition, a focus is needed on which dimensions of Rett syndrome are associated with family members' well-being. One might expect that the severity of the disability and associated increased support needs would be an important factor. However, both functional independence and adaptive behavior have not been found to be associated with maternal well-being once other factors have been taken into account (Byiers et al. 2014; Laurvick et al. 2006).

There is some evidence that the severity of the Rett syndrome phenotype may be associated with maternal well-being (Laurvick et al. 2006). In addition, unusually in the field of behavioral phenotypes, there is a psychometrically strong bespoke measure of the Rett syndrome behavioral phenotype (Mount et al. 2002). Therefore, it is important to include this dimension of behavioral phenotype severity in understanding family members' well-being. The extent of the health problems of individuals with Rett syndrome has also been associated with maternal well-being in quantitative (Byiers et al. 2014) and qualitative research (Lim et al. 2013). Data on behavioral phenotype severity and health problems need to be collected alongside a third factor that has been consistently and pervasively associated with parental well-being. In longitudinal studies (e.g., Hartley et al. 2012; Hastings et al. 2006; Herring et al. 2006; Lecavalier et al. 2006), increased severity or frequency of behavior problems of children and adults with developmental disabilities has been related to increased stress in parents over time. These associations with behavior problems have also been identified in other rare syndrome groups in cross-sectional studies (e.g., Griffith et al. 2011; Hall et al. 2007).

The aims of the present study were to: (1) Compare maternal mental health in families of individuals with Rett syndrome to normative data, (2) Compare sibling psychological adjustment in families of individuals with Rett syndrome to normative data, and (3) Explore associations between maternal well-being and three core dimensions of Rett syndrome (behavioral phenotype severity, current health problems, and behavior problems).

Method

Survey Sample

The survey methodology is described in greater detail in Cianfaglione et al. (in press). In brief, following research ethics review and approval, families were recruited through the British Isles Rett Syndrome Survey (BIRSS), an ongoing database currently maintained by the fourth author. 308 families with a daughter or son with RTT were approached and 126 (40.9 %) returned a consent form. Questionnaire packs were then distributed and families were contacted first by telephone and then by letter if they

had not returned the questionnaires within 2 months of receiving them. Ninety-three families returned completed questionnaires (30.2 % of the original 308, 73.8 % of those who consented to take part). Ninety-two participants with RTT were female and one was male. The male participant was excluded from the final sample. One participant passed away during the study and was not included in the analysis.

Sample Characteristics

The achieved sample comprised 91 girls and women with a diagnosis of RTT, of whom 80 (87.9 %) lived at home and 11 (12.1 %) lived in out of family placements. The sample was skewed towards people living in the family home. Although we sought to include only individuals living with their parents, the information on the BIRSS database was not entirely up-to-date and a minority no longer did so. Ages ranged from 4 to 47 years with a mean of 20.5 years: 43 participants were children and 48 adults. Sixty-nine had classic RTT (75.8 %), 19 atypical RTT (20.9 %) and 3 a *MECP2*-related disorder (4.3 %). Seventy-one were known to be *MECP2* positive (78.0 %): 52 in the classic group and 16 in the atypical group in addition to the three with *MECP2*-related disorder. Diagnosis of RTT was made by a pediatrician in 42.9 % of cases, a clinical geneticist in 26.4 %, by both a pediatrician and clinical geneticist in 3.3 % and by another professional in 25.3 % (this information was missing for the remaining 2.2 %). Median age of diagnosis was 3.0 years (range, 1–39 years). Diagnosis had occurred most commonly between two and 4 years of age.

Regression was reported in 87 (95.6 %). In one case (1.1 %), the mother was not sure if the child had had a regression and, in 3 others (3.3 %), all with *MECP2*-related disorder, they reported that the child did not have a regression. Mean age of regression was 18.9 months (range, 6–84 months; SD 11.75): 15 (16.5 %) had a regression before 12 months, 49 (53.8 %) between 12 and 18 months, 18 (19.0 %) between 19 and 36 months and 5 (5.5 %) after 36 months (including, one participant who had a late regression at 7 years).

Not quite all families completed the questionnaire about family experiences in addition to the questionnaire about the relative with RTT, and a very small number of fathers responded as the main parental caregiver. Therefore, in the present paper, we focus on data reported by 87 mothers (84 biological mothers, 2 foster mothers, 1 adoptive mother). The mothers were 30–70 years of age (mean 50.66 years), and for 10 families their daughter lived outside of the family home. Most mothers living with a partner (n = 73), 38.4 % were educated at least to degree level, and 44 % had annual family income of under £25,000 (roughly $40,000 USD). These mothers also completed information about 39 siblings closest in age to the RTT individual. Not all families included siblings who were children or adolescents. The included siblings were aged 2–18 years (mean 12.91, SD 4.36); 22 were male (one adoptive brother) and 17 female. Twenty-one siblings were younger than RTT individual, with 18 older.

Measures

Mothers completed the parent version of the Strengths and Difficulties Questionnaire (SDQ—Goodman 1997) to assess the psychological adjustment of the siblings. The SDQ is a widely used 25-item screening instrument for child and adolescent psychological problems. The informant responds to individual items (e.g. 'often has temper tantrums or hot tempers') by choosing between three response options ('not true', 'somewhat true', or 'always true'). Subscale scores are given for the child's emotional, conduct, peer problems, hyperactivity and pro-social (caring, helpful) behavior. The first four problem behavior domains can also be summed to give a total difficulties score. The SDQ has been validated on children from the general population in the UK (Goodman 2001) and has previously been used by researchers examining behavioral and emotional adjustment in siblings of children with disabilities (Benson and Karlof 2008; Hastings 2007).

Mothers also completed three measures of their own well-being. To measure maternal mental health, mothers were asked to complete the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith 1983). The HADS was constructed to allow a quick measure of depression and generalized anxiety in hospital settings, but has been widely used in outpatient and community research. It has been used successfully to measure depression in parents of children with developmental disabilities and maintains good reliability with this population (e.g., Jones et al. 2014). Seven of the HADS items assess depression (e.g., "I feel as if I am slowed down"), and seven measure anxiety (e.g., "I get sudden feelings of panic") and each is rated on a four point scale: *most of the time, a lot of the time, from time to time,* or *not at all.*

The Positive Gain Scale (PGS: Pit-ten Cate 2003) was used to assess positive experiences associated with raising a child with RTT. The measure consists of seven items; five relating to the perceived benefits for the mother of raising a child with ID (e.g., "Since having this child I have a greater understanding of other people"), and two focusing on what the family has gained (e.g., "Since having this child, my family has become more tolerant and accepting"). Preliminary research findings indicated that the PGS has face and content validity and a Cronbach's Alpha coefficient of .79 for parents of children with hydrocephalus and spina bifida (Pit-ten Cate 2003). The PGS has also

retained excellent reliability in other samples of parents of children with developmental disabilities (e.g., Jones et al. 2014).

Negative experiences of raising a child with RTT were measured using the Parent and Family Problems sub-scale of the Questionnaire on Resources and Stress Friedrich-Short Form (QRS-F: Friedrich et al. 1983). This scale contains 20 items assessing impact on the parent and family (e.g., "Other members of the family have to do without things because of N", and "N is able to fit into the family social group"). Parents are asked to indicate whether the items are true or false as far as they and their family are concerned. A total stress score is derived by summing the number of negatively endorsed items (i.e., positively worded items are reverse scored). Five items that have been shown to constitute a robust measure of depression in parents of children with disabilities (Glidden and Floyd 1997) were removed from the scale. This ensured that there was no overlap between the measures of stress and of mental health used in the present research.

To gather data from mothers about the three core dimensions of RTT, the following measures were used. The *Rett Syndrome Behavioural Questionnaire* (RSBQ, Mount et al. 2002) was used to assess overall severity of the RTT behavioral phenotype. The RSBQ is a 45-item checklist developed to assess behavioral characteristics of RTT. Items are rated 0–2, where 0 indicates that the item does not apply to the person with RTT, 1 sometimes true, and 2 often true. High internal consistency has been reported for the RSBQ total score (>0.90), with good inter-rater and test–retest reliability scores (>0.80) (Mount et al. 2002).

The extent of behavior problems exhibited by each individual with RTT was measured using the Parent Report version of the Developmental Behaviour Checklist (DBC—Einfeld and Tonge 2002) for children or for adults depending on the age of the individual with RTT. The DBC has excellent psychometric properties (Einfeld and Tonge 1995; Hastings et al. 2001). The DBC Total Behaviour Score was used as an index of the severity of behavior problems displayed by the girls and women with RTT.

Hall et al.'s (2008) health problems checklist was used to measure current physical health problems for the RTT individual. The checklist is a list of 15 medical problems. Mothers were asked to rate whether the person has had any of the health problems in the last month ("Have these medical problems affected your child in the last month?"). Each problem is rated from 0 (never) to 3 (severe). A current health problems score was obtained by summing the scores for the 15 items. Inter-rater reliability was .76 for the health problems in the last month (Hall et al. 2008).

Analysis

Using maternal ratings on the HADS, we explored the proportion of mothers of individuals with RTT in the sample who reported anxiety and depression above a clinical cut-off. Crawford et al. (2001) recommended using a cut-off score of >10 on either the HADS anxiety and depression scales to indicate clinical levels of problems, and also reported normative data for British women. We compared, using binomial tests, the proportions of mothers of individuals with RTT scoring 11+ on either the depression or anxiety scales of the HADS to the proportion of females in the normative sample scoring at these levels.

Focusing on the 39 siblings whose mothers rated using the SDQ, we compared their psychological adjustment with the normative SDQ parent-report sample from Great Britain (Meltzer et al. 2000). One sample t tests were used to compare mean scores from the present sample to those of the normative sample. Standardized mean difference effect sizes for mean level comparisons with normative data were also calculated for mothers' ratings of sibling adjustment. In these calculations, the normative sample SD is used because this is likely to be the best estimate of the population SD (being based on over 10,000 young people). We also compared the proportions of siblings who scored within the "abnormal" clinical range for each of the SDQ scores against the normative sample using binomial tests.

To explore the associations between three dimensions of RTT (behavioral phenotype severity, current health problems, behavior problems) and maternal well-being (anxiety, depression, stress, and positive gain), we built four multiple regression models (one for each maternal well-being measure). The three RTT dimensions were included in all four models as predictors. In addition, we included relevant demographic variables in each regression model. These demographic variables were selected via a series of univariate analyses (correlations, *t* tests) with each maternal well-being measure. All of the family demographic variables described in the Sample Characteristics section (above) were examined and retained for inclusion in a regression model if they were associated with a well-being score at $p < .05$.

Scoring rules were followed for each individual measure in the case of small numbers of missing items from any questionnaire—mean replacement was used where a minority of items were missing from a scale. Where scores were still missing, participants were excluded listwise from analyses involving scores on a missing measure.

Results

Comparisons with Normative Samples

The results of the binomial tests showed that mothers of individuals with RTT were more likely to report high levels of anxiety (24.1 %) compared to the normative sample (16 %, $p = .027$) but were no more or less likely to report high levels of depression (5.7 %) compared to the normative sample (5 %, $p = .471$).

Mean SDQ scores for siblings and proportions meeting clinical cut-off scores are reported in Table 1. On all SDQ measures (mean scores on each SDQ domain, and proportions scoring in the abnormal range), siblings of individuals with RTT in the present sample were reported as having fewer problems of psychological adjustment than British children and adolescents generally. The size of mean level differences between the RTT siblings and British children generally approached a moderate effect size, and for two SDQ domains (total difficulties, hyperactivity) the siblings in the present sample were reported by their mothers as statistically significantly better adjusted than the normative sample. A similar pattern was generally observed for the proportion of the sample within the abnormal range on SDQ scores. The RTT siblings were less likely to score in the abnormal range for all bar SDQ Hyperactivity scores. None of these differences were statistically significant when examined with binomial tests. The one difference was that a higher proportion of the RTT siblings scored into the abnormal range for SDQ pro-social behavior when compared with British norms ($p = .003$).

Regression Analyses

The results of the regression analyses are displayed in Table 2. These analyses revealed a relatively small number of associations. Specifically, an increased severity of the RTT behavioral phenotype was associated with higher levels of maternal stress and anxiety. An increased level of current health problems for the individual with RTT was associated with more perceptions of positive gain. Only one demographic variable made a significant independent contribution to the prediction of maternal well-being. Mothers reported higher levels of positive gain if their daughter with RTT resided with them rather than in an out-of-home residential placement. Overall, only a small proportion of the variance in maternal well-being was accounted for by the three measures of the characteristics of the individuals with RTT and the included demographic variables.

Discussion

Similar to previous research findings using a general health screening instrument (Laurvick et al. 2006; Urbanowicz et al. 2011), we found that mothers of girls and women with RTT reported elevated levels of anxiety compared to British normative data for women. However, these mothers were no different to a normative sample on ratings of depression. Therefore, increased psychological problems for mothers of individuals with RTT are not pervasive. Previous studies also found either no difference to normative samples or a slightly more positive well-being for a physical health score based on a standardized rating scale (Laurvick et al. 2006; Urbanowicz et al. 2011).

We also reported the first research data of which we are aware using a standardized rating scale to assess psychological adjustment in siblings of girls and women with RTT. These data provided little evidence for an increased risk of poor psychological adjustment in siblings. On the SDQ total difficulties score and all four problem domains, mothers rated siblings as having fewer problems than British children generally. Mothers did rate pro-social behavior in the siblings as slightly lower than a British normative sample, and also reported that a higher proportion than is typical had especially low levels of pro-social behaviors. It is difficult to interpret this finding in relation to pro-social behavior and it certainly requires replication. Within the present sample, the observed differences could have been determined by a very small number of children. Overall, the lack of evidence of negative impact on siblings (as reported by mothers) is even more striking when one considers that mothers in other siblings research typically report more problems than do fathers (Griffith et al. 2014), and also more problems than do siblings themselves (Hastings and Petalas 2014).

Overall, the pattern of data for mothers and siblings of RTT individuals against normative samples must be interpreted with caution. It is safe to conclude that negative impact is not pervasive. However, the extent to which mothers and siblings of RTT individuals may be at risk for negative outcomes remains unclear. This is primarily because there may be several biases operating in relation to the sample of mothers who responded to the survey. In addition, we were not able to select carefully matched comparison groups from the normative data.

The regression analyses reported in the present study are also quite unique in the field of developmental disabilities family research. We examined the independent contribution of the severity of the RTT behavioral phenotype, current severity of health problems, and current behavior

Table 1 Sibling psychological adjustment

	Normative sample (n = 10,298)		Rett siblings (n = 39)		Effect size (*d*)
	Mean (SD)	% Abnormal range	Mean (SD)	% Abnormal range	
Total difficulties	8.4 (5.8)	9.8 %	6.24 (5.45)*	5.4 %	−.37
Emotional probs	1.9 (2.0)	11.4 %	1.55 (1.70)	7.9 %	−.18
Conduct probs	1.6 (1.7)	12.7 %	1.26 (1.67)	12.8 %	−.20
Hyperactivity	3.5 (2.6)	14.7 %	2.37 (2.54)**	7.9 %	−.43
Peer problems	1.5 (1.7)	11.7 %	1.00 (1.56)	7.7 %	−.29
Pro-social behavior	8.6 (1.6)	2.3 %	8.36 (1.97)	10.3 %*	.15

* $p < .05$, ** $p < .01$

Table 2 Regression analyses of maternal well-being

Predictor variable	QRS stress		Positive gain		HADS anxiety		HADS depression	
	β	*p*	β	*p*	β	*p*	β	*p*
RTT current health probs	.002	.985	.228	.045	.171	.096	−.111	.326
RSBQ total score	.280	.026	−.133	.303	.244	.042	.138	.279
DBC Total score	.091	.466	−.042	.748	.186	.122	.198	.122
Child age in years	–	–	−.187	.329	–	–	–	–
Current placement	–	–	−.266	.019	–	–	–	–
Mother age in years	–	–	.047	.810	−.178	.079	–	–
Family income	–	–	–	–	–	–	−.204	.075

QRS stress F(3, 78) = 3.30, $p = .025$, R square = .113

Positive gain F(6, 74) = 2.20, $p = .052$, R square = .152

HADS anxiety F(4, 76) = 6.65, <.001, R square = .259

HADS depression F(4, 71) = 3.09, $p = .021$, R square = .148

problems as predictors of four aspects of maternal well-being. Unusually, general behavior problems did not emerge as a predictor of maternal well-being. Instead, the RTT behavioral phenotype severity predicted maternal stress and anxiety. More current health problems for the individual with RTT predicted increased levels of perceived positive gain. Both of these findings are in need of further research. More bespoke measures (like the RSBQ—Mount et al. 2002) of the behavioral phenotype in other rare genetic disorders could be developed and explored in relation to family well-being. It may be that these specific challenges more generally predict family responses to raising a child with a rare syndrome. There is also a need to better understand parents' positive perceptions and how these might function to enhance (or not) broader well-being. Some theoretical perspectives can also be used to predict the presence of increased positivity in the face of increased challenge (Hastings and Taunt 2002).

It is also important to consider additional limitations of the present research when interpreting the findings. Altogether, the sample of mothers of individuals with RTT was small—although this is still the second largest sample for which parental well-being data have been reported. In addition, the sample of siblings was even smaller (mainly because the SDQ is limited in terms of applicable age range—not being suitable for young adult and adult siblings). Therefore, one must be careful in drawing conclusions about the population of families of individuals with RTT. The sample was also not fully population-derived even though families were recruited from a national database.

Source variance is also a limitation with mothers providing reports about their daughter with RTT, their own well-being, and siblings' psychological adjustment. Multiple informant methods are needed in RTT family research in future. In addition, longitudinal designs are needed to be able to establish directions of effect especially for the relationship between maternal well-being and the severity of the RTT behavioral phenotype. In particular, the question of whether stress in the family might increase the risk for a more severe RTT behavioral phenotype over time would have profound implications for family support. Further research is also needed to understand how family members' adaptation changes through the natural course of

RTT. For example, how do families cope and how are they affected psychologically during a period where girls with RTT regress and lose some of their skills?

A final issue for future research is the possibility of more fine-grained analysis of genotypic sub-groups in relation to family outcomes. Within the present relatively small study, we focused on the severity of the RTT phenotype in relation to outcomes for parents and siblings. With a larger sample, it would also be possible to examine whether family experiences differ based on broad diagnostic category (e.g., classical RTT vs. atypical) and/or based on the nature of a *MECP2*-related disorder. Such research would help in establishing whether the severity of the RTT phenotype is the key variable (as suggested in the present research).

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