Change over a 16 month period in the psychological well-being of mothers of girls and women with Rett syndrome

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Abstract

Purpose. There is an emerging research literature on the experiences of family members of girls and women with Rett syndrome (RTT), but a lack of longitudinal data.

Methods. Fifty mothers whose daughters had RTT were surveyed 16—17 months after an earlier cross-sectional study. Measures completed at both time points focused on maternal positive and negative psychological well-being and their daughters' behavioural and emotional problems and RTT behavioural phenotype severity.

Results. Maternal stress, anxiety and depression demonstrated at least moderate levels of stability. Maternal positive perceptions were also moderately stable over 16—17 months. Longitudinal analyses suggested that their daughters' behavioural and emotional problems rather than RTT behavioural phenotype severity predicted later maternal well-being.

Conclusion. Mothers with RTT daughters experience chronic stress (persisting over time) but also ongoing positive perceptions. Practitioners should recognise positive perceptions, and also consider targeted behavioural parent training to reduce behaviour problems in individuals with RTT.

Rett syndrome (RTT) is a rare genetic disorder most commonly caused by a mutation in the methyl-CpG binding protein-2 (*MECP2*) gene, located on the X chromosome at *Xq28* [1], although RTT remains a clinical rather than a molecular diagnosis [2]. RTT is associated with severe to profound intellectual disability and a range of other impairments including social and communication limitations [3], developmental regression/loss of skills, motor difficulties, and stereotyped hand movements [2]. Given this array of difficulties, likely leading to challenges for carers, it is not surprising that researchers have shown increased stress and mental health problems in parents (especially mothers) of individuals with RTT compared to normative samples of adults [4, 5, 6, 7, 8], and some indication of increased relationship problems compared to parents of children with other disabilities [9].

Not all parents of individuals with RTT report increased levels of psychological distress. For example, Cianfaglione et al. [5] found that 24.1% of mothers of women and girls with RTT reported symptoms of anxiety at levels above a clinical threshold, and 5.7% reported symptoms of depression at elevated levels. To understand families that may be at higher risk for psychological problems so that they can be identified and supported, it is important to examine the factors that explain some of the variance in maternal outcomes. Correlates of psychological distress in mothers of individuals with RTT have included: dimensions of the RTT behavioural phenotype such as fewer physical health complications, fewer stereotypies, and fewer breathing problems [6]; the financial burden of specialist equipment and use of respite care [8], and comorbid epilepsy and parents' beliefs that the individual with RTT may be in pain [4]. In a cross-sectional survey, Cianfaglione et al. [5] found that the severity of the overall RTT behavioural phenotype, assessed using the Rett Syndrome Behaviour Questionnaire [10], predicted increased maternal stress and anxiety.

Contrary to general intellectual disability family research findings [11] the RTT behavioural phenotype severity, rather than the individual's behaviour problems, predicted maternal psychological distress.

Existing research on the correlates of psychological distress or well-being in parents of individuals with RTT has adopted almost exclusively cross-sectional designs [4, 5, 6, 7], and other RTT family research has used retrospective reporting methods [9]. In the only study to include data gathered at more than one time point [8], use of specialised equipment and respite care in 2004 were related to maternal mental and physical health two years later. However, these analyses did not account for earlier levels of maternal well-being. Thus, the associations found are difficult to interpret. Prospective research designs are crucial if correlates of maternal well-being are to be clearly understood as risk factors that could be targeted for change in intervention studies.

The purpose of the present study was to use a short term longitudinal follow-up of the Cianfaglione et al. [5] sample of mothers of girls and women with RTT to examine maternal well-being over time. Our focus was to examine the key finding from our cross-sectional analysis, but over time. Specifically, we explored whether behavioural and emotional problems or the severity of the RTT behavioural phenotype predicted maternal well-being longitudinally. Our secondary aim was to examine the stability of dimensions of psychological well-being in mothers of women and girls with RTT over a follow-up period of 16-17 months.

Method

Participants

The present study focused on 50 families from which mothers responded to the invitation to participate in a follow-up study of the original survey (see Procedure).

These 50 mothers were typically the biological mother of their daughter with RTT (n=47), with two foster mothers and one adoptive mother. The mothers were 37-70 years of age (mean 51.94 years). Most mothers were living with a partner (n=41), 38% were educated at least to degree level, and 44.4% had family income of under £25,000 (roughly $40,000 USD) per annum. For 9 families, the RTT individual lived outside of the family home. The RTT individuals' ages ranged from 7 to 48 years with a mean of 22.52 years: 20 of the individuals with RTT were children and 30 adults at the time of the follow-up. The children were aged 7—17 years of age (mean 12.90 years), and the adults 18—48 years of age (mean 28.93 years).

Thirty eight were had a diagnosis of classic RTT, 10 atypical RTT and 2 a *MECP2*-related disorder. Forty two were known to be *MECP2* positive: 31 in the classic group and nine in the atypical group in addition to the two with *MECP2*-related disorder. Five had not been *MECP2* tested and for three individuals their *MECP2* status was unknown. Diagnosis of RTT was made by a pediatrician in 55.1% of cases, a clinical geneticist in 24.5%, by both a pediatrician and clinical geneticist in 4.1% and by another professional in 16.3% (this information was missing for one individual). Median age of diagnosis was 6.46 years (range, 1-39 years). Diagnosis had occurred most commonly between two and five years of age.

Regression was reported in 47 (three data points missing) of the individuals with RTT. Mean age of regression was 18.04 months (range, 7-48 months; SD 8.41): 8 (17%) had a regression before 12 months, 27 (67.5%) between 12 and 18 months, 10 (20%) between 19 and 36 months and 2 (4%) after 36 months.

Measures

Mothers completed three measures about their own well-being. Maternal mental

health was assessed with the Hospital Anxiety and Depression Scale (HADS) [12]. The HADS was originally developed 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 [13]. 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) [14] 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 disability (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 [14]. The PGS has also retained excellent reliability in other samples of parents of children with developmental disabilities [13].

Stressful 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) [15]. 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 [16] were removed from the scale. This ensured that there was no overlap between the measures of stress and depression in the present research.

Mothers also completed two measures of the behavioural characteristics of their daughter. The *Rett Syndrome Behaviour Questionnaire* (RSBQ) [10] was used to assess overall severity of the RTT behavioral phenotype. The RSBQ is a 45-item checklist developed to assess behavioural phenotypic characteristics of RTT. Items are rated 0 to 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), good inter-rater and test-retest reliability scores (>0.80), and validity is demonstrated by the difference in total score for RTT individuals and those with severe intellectual disability (Cohen's d = 2.15) [10].

The extent of general behavioural and emotional problems exhibited by each individual with RTT was measured using the Parent Report version of the Developmental Behaviour Checklist (DBC) [17] for children or for adults depending on the age of the individual with RTT. The DBC has excellent psychometric properties [18, 19]. The DBC Total Behaviour Score was used as an index of the severity of behavioural and emotional problems displayed by the girls and women with RTT.

Procedure

The survey methodology is described in greater detail in Cianfaglione, Clarke, Kerr, Hastings, Oliver et al. [20], and the procedure for gathering data from mothers about their psychological well-being is described in full in Cianfaglione et al. [5].

Families were recruited through the British Isles Rett Syndrome Survey (BIRSS), an on-going database currently maintained by the fourth author, with a total of 87 mothers providing data that were reported by Cianfaglione et al. [5]. Seventy-two of these original 87 families were sent a written invitation to participate in a follow-up study approximately 1.5 years after their initial participation. Fifteen families had returned initial questionnaires late and their inclusion would have reduced the follow-up period, which already was judged to be the shortest time suitable to answer the research questions. After reminders, 50 mothers responded (69% response rate). Using information on the dates mothers recorded for the completion of the postal questionnaire survey, the follow-up period was on average 16.44 months (range 15—21 months).

Statistical analysis

To ascertain any pattern of bias affecting the follow-up sample, we compared the 50 follow-up families to the remaining 37 original families on all baseline demographic variables and the five measures used in the current report as scored at the first time point. There were no statistically significant differences between the follow-up sample and the sample who did not participate in the follow-up, suggesting that there were no reasonably large differences between the participating and non-participating respondents. Given the wide age range of the individuals with RTT and the mothers, we also examined associations between these two age variables and the other study measures. There were no significant correlations with mother or RTT individuals' ages, reflecting the findings in the cross-sectional study that these age variables did not emerge as significant predictors of maternal outcomes [5].

Our secondary research aim was examined by comparing maternal well-being (stress, anxiety, depression, positive gain) between the two time points using paired

samples t-tests, and generating stability coefficients for each of these measures over the 16-17 month period. Stability coefficients were Intra-Class Correlations (ICCs) using a two-way random and absolute agreement model.

We built four multiple regression models to address our primary research aim, one for each maternal well-being measure as reported at follow-up. In each regression model, the total RSBQ score and the total DBC score from the original data collection point were entered as predictors. In addition, the Time 1 score of the relevant maternal well-being measure was entered as a predictor. In this way, any association over time between RSBQ or DBC scores and maternal well-being was examined over and above the stability in the measure of well-being.

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 – this applied to small numbers in each analysis (see *df* values in Table 2).

Results

Stability of maternal well-being

The mean scores for each maternal well-being measure at both time points, the results of a paired samples t-test comparison, and the 16-17 month stability of the scores (ICCs, with 95% confidence intervals) are displayed in Table 1. Each of the well-being dimensions demonstrated considerable stability both in terms of lack of statistically significant mean change over time and the size of the stability coefficients – although the lower end of the confidence intervals for maternal stress and positive gain suggested only moderate levels of stability. General mental health scores

(anxiety and depression) were more stable than well-being measures that are child-focused (i.e., stress associated with caring for the child, perceptions of positive gain associated with raising the child). However, even the marginally significant mean level change in positive gain scores represented only a very small difference in terms of effect size.

-----Insert Table 1 about here-----

Longitudinal regression analyses

The results of the regression analyses are displayed in Table 2. In each model, as expected given the stability of maternal well-being over time, the Time 1 score of each measure was a significant predictor of follow-up scores. Contrary to the results of the cross-sectional survey [5], the severity of the Rett syndrome behavioural phenotype at Time 1 (RSBQ total score) was not a significant predictor of maternal well-being. Instead, the overall severity of behavioural and emotion problems (Time 1 DBC total score) emerged as a significant independent predictor of later maternal anxiety and depression scores. The DBC total score did not emerge as a predictor of later maternal stress or mothers' perceptions of positive gain.

-----Insert Table 2 about here-----

Discussion

As with parents of children and adults with disabilities in general, mothers of individuals with RTT experienced stability in mental health problems over a period of 16-17 months. These data suggest that any elevated psychological distress in mothers of individuals with RTT [4, 5, 6, 7, 8] is chronic – persisting over more than a few months. Although stress associated with the child also demonstrated stability, the lower end of the ICC confidence interval suggested only moderate stability over this period suggesting that these results should be interpreted with caution. We also

reported unique data on short term longitudinal change in the perceptions of positive gain held by mothers of individuals with RTT. Again, these positive perceptions were also relatively stable across 16-17 months but as with maternal stress the lower end of the ICC confidence interval suggested moderate stability. These data are intriguing in that they suggest that positive perceptions persist over time, at least to a moderate degree. Given the lack of longitudinal studies of maternal perceptions of positive gains, these results need to be tested with further samples of families of individuals with RTT and indeed other developmental disabilities.

Results from prospective studies in the field of developmental disabilities, across the lifespan, have shown with a degree of consistency that increased frequency or severity of behavioural and emotional problems predicts later parental psychological well-being [21, 22, 23, 24]. Our longitudinal analyses confirmed a similar pattern for mothers of individuals with RTT, with earlier behavioural and emotional problems predicting later maternal anxiety and depression over and above the putative contribution of the severity of the RTT behavioural phenotype. The severity of the RTT behavioural phenotype failed to emerge as a predictor of maternal well-being over time, in contrast to results from our earlier cross-sectional analyses [5]. It is tempting to place more weight on the current longitudinal analyses, and to conclude that cross-sectional designs may lead to misleading conclusions. However, RTT behavioural phenotype severity was still associated with maternal well-being over time and in a larger sample these relationships may have been found to be statistically significant. These possibilities require replication and extension to larger samples in additional research.

In addition to the caution that the findings require replication, there are a number of design limitations with the present study that should be considered. First,

the sample was small involving 50 mothers of individuals with RTT across a wide age range. Although longitudinal RTT family research is rare, and so even a sample of 50 may be useful, it is unlikely that this sample would be representative of RTT families. Second, mothers provided data on their daughter with RTT and on their own well-being at both time points. Thus, source variance may be a problem and multiple informant methods are needed in RTT family research in future.

Combined with our earlier cross-sectional study [5] the present longitudinal analyses suggest that targeting parental (especially maternal) psychological well-being in RTT families should be an important focus for practitioners and clinical services. Stress and mental health problems may not be as elevated for mothers of RTT individuals as for parents of children with other severe disabilities. Specifically, when compared with a normative sample in our cross-sectional study mothers were more likely to have anxiety symptoms in the clinical range but no more likely to have depression symptoms in the clinical range [5]. Thus, mothers of individuals with RTT do appear to be more likely to experience mental health problems and in the present study we have shown that these problems are likely to persist over time. At the same time, it is important that professionals and agencies recognise that mothers of individuals with RTT hold significant levels of positive perceptions that are also likely to show medium term moderate levels of stability. At present, there is a poor understanding of what functions positive perceptions may serve for parents [25] but these experiences should not be neglected by professionals.

A further practical implication relates to the association over time between maternal well-being and their daughter's behavioural and emotional problems. There have been randomised controlled trial evaluations of parenting interventions showing promise in the field of developmental disabilities [26, 27] although rarely have

existing programmes been tested within families with a child with more profound disabilities (as in RTT). Adapting and testing parenting programmes for mothers and fathers of children with profound and multiple intellectual disabilities would be a fruitful future avenue for researchers. Successfully reducing their daughters' behavioural and emotional problems is likely to positively affect well-being in parents of individuals with RTT.

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Declaration of Interest

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Table 1. Stability of well-being for mothers of individuals with Rett syndrome

Well-being measure	T1 Mean (SD)	T2 Mean (SD)	t	p	Stability (ICC [95% CI])
QRS Stress	6.70 (3.22)	7.32 (3.38)	1.55	.128	.62 [.42, .77]
Positive Gain	29.43 (4.50)	28.20 (5.88)	-1.97	.054	.62 [.42, .77]
HADS Anxiety	7.82 (4.22)	7.98 (4.28)	.44	.663	.81 [.69, .89]
HADS Depression	4.69 (3.45)	4.82 (3.76)	.41	.687	.76 [.75, .92]

Table 2. Regression analyses of maternal well-being

	QRS Stress T2		Positive Gain T2		HADS Anxiety T2		HADS Depression T2	
Predictor variable	β	p	β	p	β	p	β	p
RSBQ total score	.052	.723	.214	.117	.103	.342	-.002	.983
DBC Total score	.096	.507	-.010	.943	.255	.016	.263	.029
QRS Stress T1	.568	<.001	--	--	--	--	--	--
Pos. Gain T1	--	--	.651	<.001	--	--	--	--
Anxiety T1	--	--	--	--	.625	<.001	--	--
Depression T1	--	--	--	--	--	--	.644	<.001

QRS Stress $F(3, 44) = 9.15$, $p<.001$, $R^2 = .384$

Positive Gain $F(3, 44) = 12.78$, $p<.001$, $R^2 = .466$

HADS Anxiety $F(3, 43) = 36.34$, $p<.001$, $R^2 = .717$

HADS Depression $F(3, 44) = 26.67$, $p<.001$, $R^2 = .645$