Parent Coping and the Behavioural and Social Outcomes of Children Diagnosed with Inherited Metabolic Disorders

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Abstract Objective: To explore the level of coping and management of parents of children with inherited metabolic disorders (IMD) and the relationship with children's cognitive, behavioural and social functioning.

Methods: Parents of children ($n = 22$) with confirmed IMD (glutaric aciduria type I, methylmalonic aciduria, propionic aciduria, isovaleric aciduria, glycogen storage disease, maple syrup urine disease, ornithine transcarbamylase or very long-chain acyl-CoA dehydrogenase deficiency) completed standardised questionnaires regarding psychological distress, coping and family management. Children completed cognitive assessments and parents rated their behavioural and social functioning on standardised questionnaires. Scores were compared with normative data.

Results: Most parents were coping well; 4/22 reported high levels of psychological distress. Exploratory analysis found that parent coping variables were correlated to the child's internalising symptoms, whereas family manage-

ment was related to children's externalising behaviours and social skills. No relationship was found between parent variables and cognitive functioning.

Conclusions: Parental coping and family management impact on the child's internalising symptoms and externalising behaviours, respectively. Early identification of issues in these domains may enhance referral for therapeutic interventions and family support programmes.

Inherited metabolic disorders (IMD) are individually rare but overall are diagnosed in 1:318–1:3670 live births, depending on the population (Hutchesson et al. 1998; Dionisi-Vici et al. 2002; Aygen et al. 2014). The implementation of newborn screening and initiation of earlier treatment have decreased morbidity and mortality rates (Waisbren et al. 2003; Wilcken et al. 2009), yet some children remain vulnerable to ongoing 'metabolic crises'. Parents need to constantly manage and monitor their children since poor management can affect physical and cognitive development (Hood et al. 2014), and some children may experience poor outcomes despite early treatment (Grünert et al. 2013; Waisbren et al. 2013). Thus, parents are faced with multiple stressors throughout the diagnosis period and beyond.

Parents may experience a range of emotions at the diagnostic stage, such as guilt, anger, grief, sadness and worry for the future (Weber et al. 2012). Long-term burden includes changes in lifestyle due to dietary constraints, medication regimes and frequent visits to the medical centre – all of which affect family routines, relationships and parenting styles (Cederbaum et al. 2001; Hatzmann et al. 2009). IMD can lead to financial burden as much as emotional burden (Gramer et al. 2013). Some parents also report a type of 'social burden' regarding what friends, family and society may think about them and their parenthood

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Fig. 1 Conceptual model of biological and environmental variables that influence developmental outcomes of children with IMD

(Saleem et al. 1998). Those with a high level of social support will feel less stressed and more equipped to manage the child's condition (Hatzmann et al. 2009; Torkelson and Trahms 2010).

Stress levels in parents of children with IMD are related to competence in managing the disorder, social isolation and emotional strain (Dellve et al. 2006). Parents of children with maple syrup urine disorder (MSUD) (Packman et al. 2012), glycogen storage disease type I (GSD) (Storch et al. 2008) and urea cycle disorders (Cederbaum et al. 2001; Packman et al. 2012) experience high levels of anxiety concerning the future, dietary management and fear of death. Whilst some parents struggle, others report positive feelings of bringing the family closer together and increased compassion (Cederbaum et al. 2001).

Parental stress and its impact on family function affect the development and well-being of healthy children (Fisak et al. 2012), as well as those with chronic illness (Thompson et al. 1999; Immelt 2006; Knafl et al. 2007). Parental stress affects glycaemic control in children with type I diabetes mellitus (Tsiouli et al. 2013) and behaviour and social development in children with cancer (Colletti et al. 2008; Hilliard et al. 2011) and with spina bifida (Friedman et al. 2004). Parents of children with PKU reported their families were less cohesive and adaptive compared with parents of healthy children (Kazak et al. 1988), yet no differences were found in GSD I (Storch et al. 2008). Parents of children with MSUD reported that the burden of responsibility of their child's condition impacted most on their family relationships (Packman et al. 2012). However, findings regarding the impact of family functioning on child outcomes are equivocal (Shulman et al. 1991; Grünert et al. 2013).

The 'double-hazard theory' proposes that children with brain insult or injury are not only susceptible to poor

cognitive, psychological and behavioural outcomes due to the impact on the brain, but they are also more susceptible to their environment. Children may also have a certain amount of 'reserve', whereby family and social support can act as a buffer to enhance outcomes (Breslau 1990; Dennis 2000). Thus, it is possible that targeting problem environmental factors offer the opportunity to modify children's cognitive, behavioural and social outcomes.

Integrating the available literature, we present a biopsychosocial model to conceptualise the various factors that contribute to child outcomes in IMD (Fig. 1). The model incorporates biological (e.g., central nervous system involvement) and disorder-related factors (such as age at diagnosis), as well as environmental (family stress levels, ability to manage complex treatment regimens, etc.). We suggest that the contribution of these factors differs across disorders, with a key factor being timing of diagnosis (e.g., newborn screening versus clinical diagnosis).

In the present study, we explored the impact of the environmental factors, specifically the level of coping and well-being of parents of children with IMD and their family management. We also explored whether parent functioning was related to cognitive, social and behavioural outcomes in their children.

Method

Participants

Families were identified via Victorian Inborn Errors of Metabolism (VICIEM), an in-house metabolic databank. Inclusion criteria were parents of children (1) with

Table 1 Diagnosis of children in the sample (*n*)

Inherited metabolic disorder diagnosis	<i>n</i>
<i>Newborn screening</i>	
Methylmalonic aciduria (MMA) mut ^o	1
Isovaleric aciduria (IVA)	1
Propionic aciduria (PA)	1
Glutaric aciduria type I (GA I)	6
Maple syrup urine disease (MSUD)	1
Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency	6
<i>Clinically diagnosed</i>	
Glycogen storage disease (GSD) type Ia and Ib	2
Glycogen storage disease (GSD) type III	1
Isovaleric aciduria	1
Ornithine transcarbamylase (OTC) deficiency	2
Total	22

mut^o: this is the mutation type mut^o (as opposed to mut-)

confirmed glutaric aciduria type I, methylmalonic aciduria, propionic aciduria, isovaleric aciduria, glycogen storage disease, maple syrup urine disease, ornithine transcarbamylase or very long-chain acyl-CoA dehydrogenase deficiency via newborn screening or diagnosed clinically (Table 1) and between 3 and 16 years of age; (2) not diagnosed with any other medical condition that could interfere with the interpretation of results; and (3) patients at Royal Children's Hospital (RCH) in Melbourne, Australia.

Measures

Parent Mental Well-Being

Kessler 10 Psychological Distress Scale (Kessler et al. 2002) Kessler 10 is a 10-item measure of parent anxiety and depression during the past 4 weeks. Respondents rate each item based on 5-point scale where 1 indicates none of the time, and 5 indicates all of the time. Scores were categorised based on standard cut-off values: low (10–15), moderate (16–21), high (22–30) and very high (31–50) psychological distress. It has been shown to be superior as a screener for mental disorders, good construct validity (Andrews and Slade 2001; Slade et al. 2011) and excellent reliability of 0.94 (Donker et al. 2010).

Parent Coping and Support

Parent Experience of Childhood Illness (PECI) Short Form (Bonner et al. 2006) The Peci is designed to assess emotional adjustment, coping and perceived level of support available, in the primary caregiver of children who have a chronic illness. It contains 25 questions and

four scales: guilt and worry, unresolved sorrow and anger, long-term uncertainty and emotional resources. Higher scores indicate greater distress or poorer coping except for on emotional resources, which indicates a higher level of support. It demonstrates acceptable reliability between 0.72 and 0.89 (Bonner et al. 2006).

Family Functioning and Management

Family Management Measure (FaMM) (Knafl et al. 2011) The FaMM is constructed to measure family functioning and management in families who have a child with a chronic illness. It contains six subscales with 45 questions: child's daily life, condition management ability, condition management effort, family life difficulty, view of condition impact and parent mutuality. For the current study, we excluded the variables 'child's daily life' and 'view of condition impact' as we were primarily concerned with the parents' view of only their family and to reduce variables. The FaMM has good internal consistency ranging from 0.72 to 0.90 for mothers (Knafl et al. 2011) and has been validated in Australian samples (Hutton et al. 2012).

Behaviour, Emotional and Social Functioning

Strengths and Difficulties Questionnaire (SDQ) (Goodman 2001) The SDQ is a widely used measure of behaviour, emotional and social functioning that is completed by a parent regarding their child aged between 3 and 16 years. It assesses emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behaviour. Higher scores indicate more problematic behaviours except for prosocial behaviour where higher scores indicate positive behaviours. The parent form contains 25 items, and scores for each subscale are categorised into normal, borderline or abnormal according to Australian norms (Mellor 2005).

Intelligence

Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler 1999) and **Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI-III)** (Wechsler 2002) Intelligence was assessed using the Wechsler scales for the appropriate age range ($M = 100$, $SD = 15$).

Demographic Questionnaire, Socioeconomic Status and Background Medical History A questionnaire was administered to gather information about family, developmental and medical history. Socioeconomic status (SES) was assessed using deciles (1–10) from the Socio-Economic Index of Areas (SEIFA) 2011 data (ABS 2013b). These are calculated using census data from a number of

variables based on the population demographics of the area postcode, with 1 representing the lowest 10% of areas.

Statistical Analysis Exploratory analyses were conducted using Statistical Package for Social Sciences (SPSS) for Windows (version 18). Due to the small sample size and nonnormal distributions, exploratory nonparametric statistical analysis was utilised. It should be emphasised that this analysis was exploratory, and therefore correlations do not represent causal relationships. Spearman correlation coefficients (r_s) are reported for the relationship between parent coping and child outcomes. As both the PEGI and FaMM are measures intended for parents of children with chronic illness, no normative data are available. For comparison, PEGI scores are presented with results from parents of children with brain tumour from the test authors (Bonner et al. 2006). FaMM scores are presented with the results from parents of children with diabetes, also from the authors of the test (Rearick et al. 2011).

Procedure

The study protocol was approved by the Human Research Ethics Committee at the RCH (HREC #32218A). Parents were sent information letters, and once informed consent was received, they were invited to complete the study questionnaire. Most parents were part of a larger study of neurodevelopmental outcomes where children completed a full neuropsychological assessment, and some parents only completed the questionnaire component ($n = 4$).

Results

Thirty-nine patients were identified through the VCIEM database. Seven children were too young and ten families declined or did not return study questionnaires. There were 16/22 male patients (72%). Only one parent per family responded to the questionnaire (total $n = 22$; age range 28–50 years). SES ranged from 1 to 10 ($m = 6.60$, $SD = 2.70$). The average number of hospitalisations was 10.41 ($SD = 12.62$). Based on respondents' answers, 18/22 (82%) children resided with both parents, and four (18%) resided with their mother only (three separated from father, one deceased), reflecting proportions similar to those reported in the Australian population (ABS 2013a). Only one child, with GA I and diagnosed through newborn screening, was classified as intellectually disabled (<70).

Parent Mental Well-Being

Responses on the Psychological Distress Scale ($M = 17.05$, $SD = 8.24$) showed 16/22 parents were well adjusted, two parents were in the moderate risk range, one was in the

high-risk range, and three were experiencing very high-risk levels of distress (children were diagnosed with GSD, MMA, VLCAD and OTC deficiency). Only one parent reported a history of previous depression. Of the four mothers that reported the highest distress, three had children diagnosed clinically.

Parent Coping and Family Management

Overall, parents of children with IMD showed better coping than parents of children with a brain tumour (Table 2). Whilst there were a number of parents with higher scores in comparison to the paediatric brain tumour group, three parents reported levels well above the mean, indicating that, whilst most parents were coping well, some parents were experiencing high levels of negative emotions associated with the IMD.

Scores on the FaMM were compared to those from parents of children with diabetes (Rearick et al. 2011) and were found to be similar (Table 2).

Child Outcomes

Children ($n = 18$) had IQ scores mostly within the average range ($M = 100.67$, $SD = 17.53$). There was no relationship found between child IQ and any of the parent distress, parent coping or family management variables. There was also no significant correlation between SES and child outcomes, although the relationship with peer problems approached significance ($p = 0.055$).

Child Behaviour and Emotional Problems (SDQ)

Results from the SDQ (Table 3) indicate that a proportion of children were displaying behaviour problems within the 'abnormal' range, which is considered to be of clinical significance (Goodman 2001; Mellor 2005). Three children of the four mothers who reported the highest distress had emotional symptoms in the abnormal range (one diagnosed through newborn screening, two diagnosed clinically).

Child's emotional symptoms such as depression and anxiety were positively correlated with parent psychological distress ($r_s = 0.47$, $p = 0.03$) and negatively correlated with parent emotional resources ($r_s = -0.42$, $p = 0.05$).

Child's conduct problems were positively correlated with condition management effort ($r_s = 0.48$, $p = 0.02$) and family life difficulty ($r_s = 0.43$, $p = 0.05$). Child's hyperactivity was positively correlated with condition management effort ($r_s = 0.61$, $p = 0.003$) and family life difficulty ($r_s = 0.61$, $p = 0.002$) and negatively correlated with condition management ability ($r_s = -0.46$, $p = 0.03$) and emotional resources ($r_s = -0.50$, $p = 0.02$).

Table 2 Parent mean scores of self-reported coping and emotional resources (PECI) and family management mean scores (FaMM)

	Possible score range	Paediatric brain tumour group ($n = 148$) ^a M (SD)	Metabolic disorders group ($n = 22$) M (SD)	Parents scoring above the mean of paediatric brain tumour group
<i>PECI</i>				
Guilt and worry	0–3.82	1.72 (0.77)	1.26 (0.81)	5
Unresolved sorrow and anger	0–3.63	1.51 (0.82)	0.97 (0.81)	3
Long-term uncertainty	0–4.00	1.97 (0.87)	1.20 (0.80)	1
Emotional resources	80–4.00	2.70 (0.66)	3.05 (0.63)	7
		Diabetes group ($n = 11$) ^a	Metabolic disorder group ($n = 22$)	Parents scoring above the mean of diabetes group
<i>FaMM</i>				
Condition management ability	12–60	50.55	52.36	7
Condition management effort	4–20	13.82	10.14	4
Family life difficulty	14–70	28.27	26.14	6
Parent mutuality ^b	8–40	31.27	31.00	9

Note: $n = 22$ parents/families, only one parent completed questionnaires per family

^a Paediatric brain tumour results from original test authors (Bonner et al. 2006), Diabetes group results from (Rearick et al. 2011) no SD available

^b $n = 18$ coupled parents only

Table 3 Child behavioural, emotional and social functioning ($n = 22$)

Scales	Normal (n %)	Borderline (n %)	Abnormal (n %)
Emotional symptoms	17 (77)	0 (0)	5 (23)
Conduct problems	16 (72)	3 (14)	3 (14)
Hyperactivity	14 (64)	2 (9)	6 (27)
Peer problems	15 (68)	1 (5)	6 (27)
Prosocial behaviour	18 (82)	3 (14)	1 (4)

Child Social Skills

Peer problems were not correlated with parent coping or family management variables. Prosocial behaviours on the SDQ were negatively correlated with condition management effort ($r_s = -0.48$, $p = 0.02$), suggesting that parents who indicated lower levels of effort required to manage the IMD rated their children as having higher levels of prosocial behaviours, such as sharing with others and considering others' feelings.

Discussion

The aim of the current study was to investigate coping and family management in a cohort of parents of children with IMD by exploring the relationship between parent func-

tioning and child's cognitive, social and behavioural functioning. The results suggest that most parents were coping and managing well. Parent coping and family management were related to child behavioural and emotional outcomes and prosocial behaviours. However, no such relationship was found with cognitive outcomes.

Most parents of children with IMD in our cohort did not demonstrate elevated psychological distress according to Australian normative data, yet in a small number of parents, levels of psychological distress fell in the 'at risk' range and three parents fell in the clinically significant range (>30). Three of the six parents of children diagnosed clinically had high psychological distress scores. The interaction between the child's disorder factors, such as the age at diagnosis, potentially impacts upon parent stress; however, the number of families is too small to draw robust conclusions. The difference in parental stress between those with children diagnosed clinically and those diagnosed by newborn screening has been alluded to previously (Waisbren et al. 2003).

Some parents reported higher levels of coping in comparison with parents of children with a brain tumour (Bonner et al. 2006). This could be due to the fact that the latter may enable less time for adjustment in comparison to IMD, despite the long-term uncertainty in both groups of disorders (Bonner et al. 2008). Family management scores were comparable to those in a cohort of parents with children diagnosed with diabetes (Rearick et al. 2011) who, like children with IMD, require lifelong management, dietary changes and a high level of parental responsibility. This is despite the fact that diabetes is more prevalent, and

there is greater public understanding and knowledge about it in comparison with IMD. We speculate that coping and family adjustment in IMD may vary over time, with more distress at diagnosis and during periods of health decline in the child. It is possible that this may also vary between parents with children diagnosed clinically and newborn screening.

It is well documented that IMD present an emotional burden to parents (Cederbaum et al. 2001; Packman et al. 2007) and that parents who may be struggling to cope potentially create greater anxiety and worry in their children (Mullins et al. 2007). In the current study, poorer parent coping was associated with more emotional symptoms in children, and poorer family management was associated with more externalising behaviours such as conduct problems and hyperactivity in children. The link between family management and externalising behaviours was the strongest in our study, consistent with previous reports in parents of children with MSUD (Packman et al. 2007). Similarly, in families of children with spina bifida, family functioning predicted child externalising behaviour, whereas parental functioning predicted child internalising symptoms (Friedman et al. 2004).

This significant relationship suggests parent coping and family management are particularly salient to child emotional and behavioural outcomes, in accordance with our model. As there are no other studies that have investigated this relationship, results should be considered as preliminary and interpreted with caution as correlations are exploratory in nature and do not indicate causal relationships. Further research should aim to clarify the strength of this relationship and whether it may be reciprocal as suggested by findings in other populations such as traumatic brain injury (Taylor et al. 2001). It is important to note the potential protective value of parent emotional resources on child outcomes, as is apparent from these results.

Prosocial behaviours were related to family management, in support of our model. Previous reports of social outcomes in children and adults with an IMD suggested that they may be vulnerable to social problems (Storch et al. 2008; Packman et al. 2012; Grünert et al. 2013). The role of parents and family functioning in relation to child social outcomes is well established (Yeates et al. 2007). For example, parental stress is related to child's social adjustment (Colletti et al. 2008). Families who are coping better with the disorder may have more opportunity for family social outings, and children therefore have more social experiences.

No relationship was found between child cognitive functioning and any of the parent variables. This is consistent with recent research on children with propionic aciduria (Grünert et al. 2013). It is possible that in some

disorders the biological-pathological factor is the strongest, regardless of the mode of diagnosis and parental management. There was also no relationship between SES and child outcomes, conflicting previous research that found a relationship between SES and depression in PKU children (Wu et al. 2011), possibly because of the difference between countries or due to different measures or age groups.

The main limitation of the study was a small sample size that affects power and statistical analysis. Larger sample sizes and longitudinal data would enable further statistical validation and exploration of predictive factors. A major limitation in this, and other studies, is the use of parent self-report questionnaires, which can be unreliable as parents may be biased in their responses, at times underestimating their own stress levels (Read 2003) and overestimating their child's abilities (Gramer et al. 2013). Future studies should include additional respondents (e.g., teacher, self-report) and compare responses from mothers and fathers.

Conclusion

Our results suggest that whilst most parents of children diagnosed with an IMD may cope well and their families are managing, there are a small number of parents who may not adapt as easily and this may impact on the child's behaviour and social outcomes, as proposed by our model. Questionnaires such as the PEGI and FaMM may be utilised to screen parents within the clinical setting. This study highlights the need for a multidisciplinary team for supporting families and to consider biopsychosocial factors.

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Take-Home Message

Most parents report coping well with having a child with IMD. However, a small subset may not adapt as easily, potentially impacting on child behavioural outcomes.

Compliance with Ethics Guidelines

Conflict of Interest

Amy Brown, Louise Crowe, Avihu Boneh and Vicki Anderson declare no conflict of interest.

All procedures followed were in accordance with the ethical standards of responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as advised in 2000 (5).

Informed consent was obtained from all patients for being included in the study. Ethics approval was granted from the RCH Human Research Ethics Committee (HREC #32218A).

Details of the Contributions of Individual Authors

Amy Brown recruited patient subjects, performed neuropsychological assessments, devised a study protocol, collected data and wrote and edited the manuscript.

Louise Crowe participated in discussions about the manuscript and assisted in reviewing and editing the manuscript.

Avihu Boneh participated in devising a study protocol, discussions about the manuscript and reviewing and editing the manuscript.

Vicki Anderson participated in devising a study protocol, discussions about the manuscript and reviewing and editing the manuscript.

Details of Previous Publication

- Abstract originating from this manuscript has been accepted for poster presentation at the SSIEM Annual Symposium, Lyon, France, September 2015.
- Cognitive and behaviour scores of children with glutaric aciduria type I and very long-chain acyl-CoA dehydrogenase deficiency are reported in the following articles:
 - Brown A, Crowe L, Beauchamp MH, Anderson V, Boneh A (2014) Neurodevelopmental profiles of children with glutaric aciduria type I diagnosed by newborn screening: a follow-up case series. *JIMD Reports* 18:125–134
 - Brown A, Crowe L, Andresen BS, Anderson V, Boneh A (2014) Neurodevelopmental profiles of children with very long-chain acyl-CoA dehydrogenase deficiency diagnosed by newborn screening. *Mol Genet Metab* 113(4):278–282

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