

Factors associated with behaviors measured by the Rett Syndrome Behaviour Questionnaire in Rett syndrome

Jenny Downs,^{1,2} Damian May,³ Kingsley Wong,¹ Helen Leonard¹

¹ Telethon Kids Institute, The University of Western Australia, Australia; ² School of Allied Health, Curtin University, Perth, Australia; ³ Acadia Pharmaceuticals

BACKGROUND

- Abnormal behaviors are a feature of Rett syndrome (RTT), beyond the core diagnostic features.
- The Rett Syndrome Behavior Questionnaire (RSBQ) evaluates behaviors in RTT (1).
- It has been used in recent clinical trials testing mecaseprin and trofinetide for RTT, e.g., (2,3).
- Some behaviours measured with the RSBQ vary with genotype (4) but there are few other data that evaluate effects on RSBQ scores.

Aims

To investigate relationships between genotype, age, walking ability, sleep and RSBQ scores in RTT.

METHOD

Study design

- Observational study, participants in the International Rett Syndrome Database, InterRett, who completed the 2018 follow up questionnaire.

Dependent variables

- RSBQ total scores, general mood and fear/anxiety subscale scores.

Independent variables

- Genotype, age-group (<12y, 12-18, 19-29, >28y), functional abilities (walking) and sleep (Sleep Disturbance Scale for Children (5); insomnia and excessive daytime sleepiness subscale T scores categorized as normal or abnormal)

Analysis

- Relationships estimated with multivariate linear regression.

RESULTS

Participants (n=210)

- Median age 18y2m (range 6-51y).
- Approx. 1/3 could walk independently.
- insomnia and sleepiness scores indicated dysfunction in 26% and 18%, respectively

RSBQ Scores

- Total (max possible /135)
 - Mean (SD) 32.1 (13.3), range 6-88.
- General Mood subscale (max possible /16)
 - Mean (SD) 4.7 (3.7), range 0-16.
- Fear and Anxiety subscale (max possible /8)
 - Mean (SD) 3.0 (2.0), range 0-8.
- Scores for subcategories of age, genotype, walking, insomnia and daytime sleepiness T scores shown in Table.

Associations between independent variables and RSBQ scores (higher scores = greater severity)

Age

- Total, mood, and fear/anxiety scores decreased in teenagers and adults, compared to children <12y.

Genotype

- Individuals with the p.Arg294* mutation had higher fear/anxiety scores (coeff 1.6, 95%CI 0.00,3.10), compared with the p.Arg270* mutation.
- Otherwise, no particular relationships.

Walking

- Compared to being unable to walk,
 - Higher total and fear/anxiety scores if assisted walking a
 - Higher mood scores if independent walking.

Insomnia and daytime sleepiness

- Total, mood, and fear/anxiety scores higher with insomnia and daytime sleepiness T scores >70.

Variables	N (%)	RSBQ scores – mean (SD)			
		Total	Mood	Fear/Anxiety	
Age (y)	<12	33 (15.7)	40.1 (14.9)	6.7 (3.9)	4.3 (2.2)
	12-18	87 (41.4)	32.6 (14.8)	4.5 (3.8)	3.1 (1.9)
	19-28	52 (24.8)	30.7 (10.9)	4.6 (3.7)	2.8 (2.1)
	>28	38 (18.1)	29.8 (11.2)	4.7 (4.0)	2.1 (1.5)
Genotype	p.Arg270*	11 (5.2)	35.4 (19.0)	5 (4.6)	3.2 (1.8)
	C-terminal del.	19 (9.1)	30.2 (7.7)	3.7 (3.1)	3.0 (1.7)
	Early trunc.	14 (6.7)	29.9 (12.6)	3.7 (4.0)	2.4 (2.1)
	Large deletion	14 (6.7)	32.8 (15.9)	4.9 (3.7)	2.6 (2.2)
	p.Arg106Trp	11 (5.2)	33.0 (14.2)	5.1 (4.3)	3.0 (1.9)
	p.Arg133Cys	16 (7.6)	30.5 (16.2)	4.8 (4.3)	2.7 (1.7)
	p.Arg168*	26 (12.4)	32.5 (13.4)	4.3 (2.9)	3.2 (2.1)
	p.Arg255*	29 (13.8)	35.6 (16.0)	4.8 (4.5)	3.4 (2.2)
	p.Arg294*	14 (6.7)	35.8 (11.8)	7.6 (4.1)	4.0 (1.9)
	p.Arg306Cys	12 (5.7)	29.7 (12.7)	5.1 (3.0)	3.2 (2.1)
Walking	p.Thr158Met	22 (10.5)	35.1 (14.4)	5.4 (4.1)	3.4 (2.2)
	Other	22 (10.5)	31.3 (10.3)	5.0 (3.9)	2.7 (1.8)
	No assistance	71 (34.3)	31.3 (14.3)	5.6 (4.2)	2.5 (1.8)
Insomnia	Assisted	65 (30.9)	35.7 (13.9)	4.9 (4.0)	3.6 (1.9)
	Unable	71 (33.8)	30.9 (11.8)	4.0 (3.2)	3.1 (2.2)
Sleepiness	70 and above	55 (26.2)	39.1 (15.1)	6.4 (4.0)	3.9 (2.0)
	Below 70	150 (71.4)	30.1 (11.8)	4.2 (3.7)	2.8 (1.9)
Sleepiness	70 and above	37 (17.6)	44.5 (16.0)	6.6 (4.4)	4.6 (2.2)
	Below 70	164 (78.1)	30.0 (11.7)	4.4 (3.6)	2.8 (1.8)

CONCLUSION

- RSBQ scores do not appear to reflect severity as associated with usual markers of severity including genotype and walking.
 - Genotype results consistent with literature indicating that the p.Arg294* mutation has implications for mental health.
- Poor sleep has strong relationships with poorer behaviors reflected in the RSBQ.
- Further analyses: include more children with RTT in analyses and evaluate relationships between genotype, phenotype and alternative scale and subscale structures (6).

REFERENCES:

- Mount et al – PMID 12455930
- Kwaja et al – PMID 24623853
- Glaze et al – PMID 30918097
- Robertson et al – PMID 16389588
- Bruni et al - PMID: 9065877
- Oberman et al - PMID: 37104862

ACADIA LOGO

TELETHON
KIDS
INSTITUTE
Discover. Prevent. Cure.