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

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BACKGROUND

- Abnormal behaviours and emotional features, such as mood fluctuations or screaming at night, occur in Rett syndrome (RTT), beyond the core diagnostic features
- The Rett Syndrome Behaviour Questionnaire (RSBQ) was developed to differentiate children with RTT from those with intellectual disability but not RTT[1]
- The RSBQ has been used in recent clinical trials testing mecasermin and trofinetide for RTT[2,3]
- Some behaviours measured with the RSBQ vary with genotype[4]

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 (higher scores = greater severity)

- 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-group, genotype, walking, insomnia and daytime sleepiness T scores shown in Table

Variables		N (%)	RSBQ scores – mean (SD)		
			Total	Mood	Fear/Anxiety
Age-group (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)
	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)
Walking	No assistance	71 (34.3)	31.3 (14.3)	5.6 (4.2)	2.5 (1.8)
	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)
Insomnia	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)

Associations between independent variables and RSBQ scores

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
  - 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

CONCLUSION

- Severity of RSBQ scores in this population do not appear to reflect severity in other markers of severity including genotype and walking
  - Genotype results consistent with literature indicating that the p.Arg294* mutation has implications for mental health
- Poorer sleep has strong relationships with poorer behaviours reflected in the RSBQ
- Further analyses: include more children in analyses and evaluate relationships between genotype, phenotype and alternative scale and subscale structures[6]

REFERENCES:

1 Mount et al – PMID 12455930; 2 Khwaja et al – PMID 24623853; 3 Glaze et al – PMID 30918097; 4 Robertson et al – PMID 16389588; 5 Bruni et al - PMID: 9065877; 6 Oberman et al - PMID: 37104862

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