Cortisol Response to Standardized Pain and Sensory Examinations in Rett Syndrome

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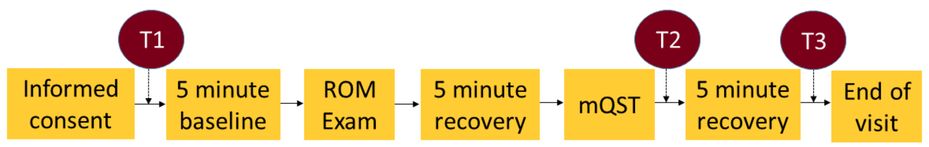
Introduction

- Rett syndrome (RTT) is a severe, neurodevelopmental syndrome associated with severe deficits in communication and motor skills.
- Mutations of the methyl-GpG-binding protein 2 (MECP2) gene account for most cases of RTT.[1]
- Several studies in animal models of RTT have shown abnormal stress responses, characterized by excessive cortisol responses to stress.[2,3]
- There is limited information on stress responses in clinical samples in this population, likely because It is difficult to identify stress paradigms due to ethical and practical limitations.
- In the current study, we investigated cortisol responses to two standardized designed to investigate musculoskeletal pain status (range of motion [ROM] exam) and somatosensory function (modified quantitative sensory test [mQST], respectively.

Methods

- Data from 14 participants with clinical diagnoses of RTT were included. Participants were recruited from Gillette Children's Specialty Healthcare RTT clinic, and visits were scheduled before or after standard of care clinical appointments at Gillette.
- Each research visit followed a standard sequence (maroon circles represent saliva sampling time points):



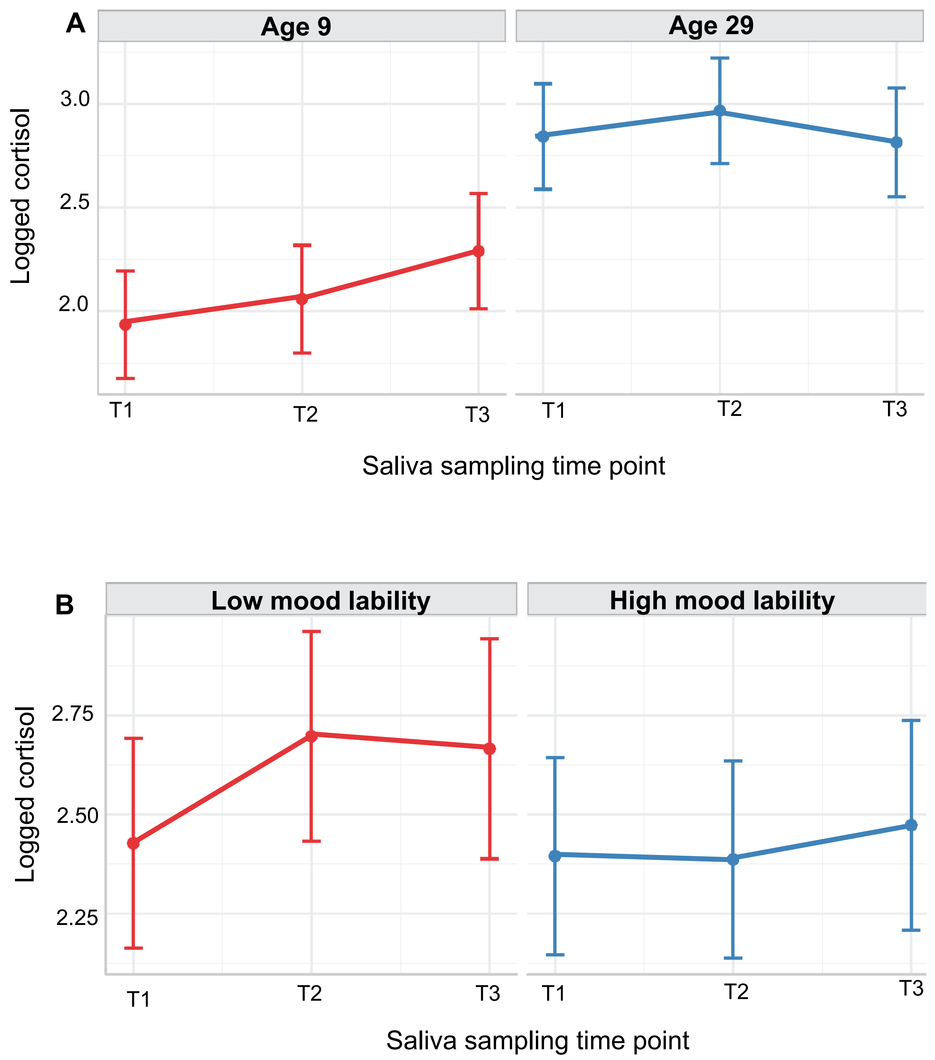
- The ROM consisted of the examiner moving the participant's head, arm, and leg joints through their full range of motion.
- The mQST consisted of the application of 6 tactile stimuli to the participant's hands and feet.
- Based on the known time course of cortisol responses to stress, T2 should reflect the response to the ROM exam, and T3 should reflect the response to the mQST.
- Mood lability symptoms were assessed using the DASH-II.[4]
- Linear mixed models evaluated changes in cortisol across the three samples, and differences in patterns based on age and parent-reported mood lability symptoms.

Clinical characteristics of participants

ID	Age (years)	MECP2 mutation	Seizures	Mood score
1	4	P152R	No	12
4	11	S49X	Yes	9
10	25	R133C	Yes	10
12	23	R294X	No	8
13	23	R294X	Yes	3
15	20	K144X	Yes	3
16	30	N/A	No	10
17	15	T158M	Yes	15
19	16	P272X	Yes	9
21	37	N/A	Yes	6
22	16	P322L	Yes	4
23	13	Ins/del	Yes	10
25	15	Deletion	Yes	3
27	8	R270X	No	5

Results

Predicted values of cortisol across the three time points by age (A) and mood lability symptoms (B).



Linear mixed model results

Term	F-value	DF	p-value
Intercept	904.28	1,34	<.0001
Time point	3.10	2, 34	.058
Age	23.12	1, 6	.003
Mood lability	0.30	1, 6	.603
Time point * Age	4.45	2, 34	.09
Time point * Mood lability	3.62	2, 34	.038

Conclusions

- Significant differences in cortisol patterns were observed across different levels of age and mood symptoms.
- The results suggest that a combination of a standardized ROM and mQST can be used to elicit cortisol responses in this population, but additional work is needed to understand whether the two components produce independent cortisol responses
- Levels of cortisol overall were significantly associated with age, which is consistent with the general popualation[5]
- Younger individuals appear to show cortisol reactions to both the ROM and QST, whereas older individuals show responses only to the ROM.
- Individuals with high lability appeared to react more to the mQST, whereas those with low lability showed greater changes in response to the ROM
- The small sample limits the generalizability of the findings.
- Future research should examine relationships between cortisol reactivity and other indices of stress reactivity (e.g., behavioral indices, heart rate, electrodermal activity) within the visit

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