Testing Two Observational System Approaches to Measure Behavioral Reactivity During Modified Quantitative Sensory Testing in Rett Syndrome

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Introduction

Background

The behavioral phenotype for Rett syndrome (RTT), a rare neurodevelopmental disorder, is characterized by myriad health issues and despite the diagnostic criteria of pain insensitivity,[1] there is contrary evidence for intact pain expression.[2,3]

Most individuals with RTT cannot verbally self report, therefore accurately evaluating pain remains difficult and our understanding of basic tactile and nociceptive (pain) function is limited.

Purpose

The purpose of this study was to develop an observational coding system based on a non-verbal pain scale (the Pain + Discomfort Scales[4]; PADS) to measure pain- and discomfort-related behavioral reactivity as a potential sensitive, clinic-friendly outcome measure for clinical trials.

Specifically, we compared two different direct observational coding approaches during a quantitative sensory testing procedure.

Methods

Participants

20 girls and women with RTT syndrome or a MECP2-related disorder (M age = 15.9 years)

Procedures

We conducted a modified quantitative sensory test (mQST) comprised of six calibrated tactile and nociceptive stimuli applied to the hands and feet: light touch, pin prick, cool, pressure, repeated Von Frey, and heat[5].

Analyses

We quantified behavioral reactivity using a modified version of the PADS (see Table 1 for specific behaviors coded).

We coded the same videos two different ways:

1. Individual behaviors (e.g. brow furrow) scored 0 - 2 for each application of each stimulus
2. Behavioral classes (e.g. vocal) scored 0 - 3 combining all applications for each stimulus

Total score reactivity and reactivity by stimuli were were compared using a Spearman correlation, due to non-normal distribution of scores.

Supported, in part, by NIH Grant No. 69985, Mayday Fund

Results

Table 1. Behaviors Coded

Vocal	Any sound made by the participant, including yell, moan, or cry. Excludes body function (e.g. burp).
Facial	*Upper:* brow raise, brow furrow, change in eyes (e.g. rapid blinks, squeezed shut) *Lower:* mouth stretch, mouth open, tongue thrust, lip pucker, teeth grind
Body	Flinch, moving away from stimulus, guarding
Physiology	Audible inhale or exhale, tears, gasp. Excludes body function (e.g. cough)

Total Score Comparison

Figure 3. Total scores from both methods (r = 0.75, p < 0.0001).

Reactivity by Stimulus

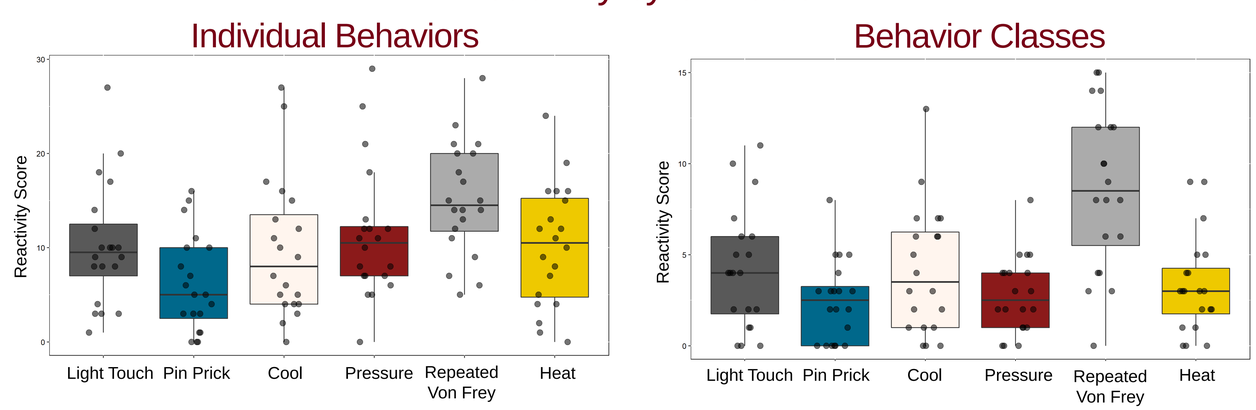

Figure 1. Total reactivity scores for each individual for each stimulus for both scoring methods. Black bar indicates the mean and error bars indicate the first and third quartile on the boxplots. Each point represents one person.

Reactivity by Type of Behavior

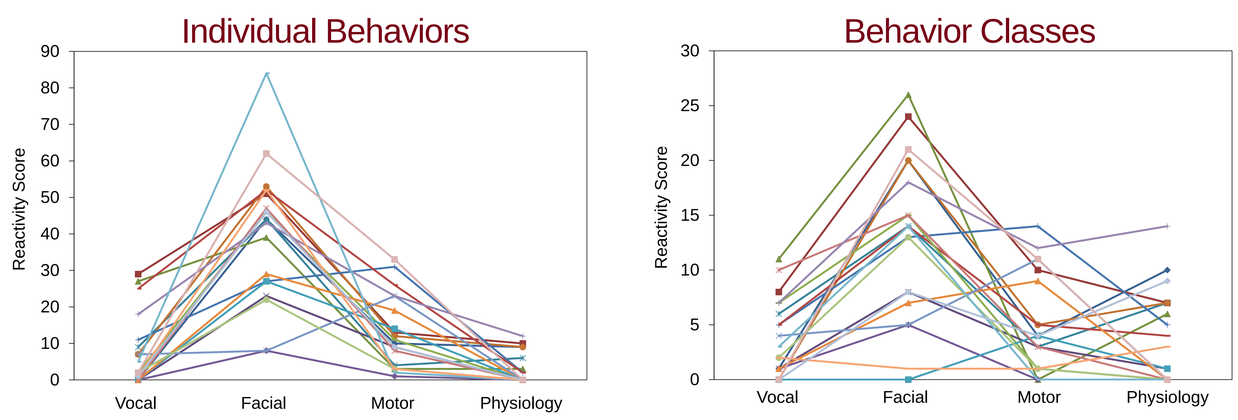

Figure 2. Total reactivity scores by the type of behavior for both scoring methods. Each line is one participant.

Table 2. Stimuli Correlations

	Light Touch	Pin	Cool	Pressure	Repeated Von Frey	Heat
Spearman's rho	0.69*	0.74*	0.67*	0.25	0.88*	0.60*
p	0.001	< 0.0001	0.001	0.28	< 0.0001	0.005

* Significant at p ≤ 0.05.

Discussion

Both methods quantified pain- and discomfort-related behavior in RTT (Fig 1, 2). Total scores and scores by all stimuli except deep pressure were at least moderately positively correlated and showed similar response patterns (Fig 3, Table 2), indicating that scoring classes of behavior may be sufficient to describe sensory behavioral reactivity in RTT.

An advantage to the 'scoring classes of behavior' method is that it takes significantly less time (several months) for coders to reach a high reliability standard. The approach also reduces the time needed to code one participant's protocol, saving both time and financial resources during training and data analysis.

Although there are increasing advances in automated facial coding, automated methods also present challenges, such as head position requirements, and lack the inclusion of vocal, gross motor, and physiological signs of reactivity.

With the move from mouse to human and the increasing number of clinical trials in RTT, a valid and reliable pain- and discomfort- based scoring method may provide a sensitive endpoint, as well as a way for further research to investigate somatosensory and nociceptive function in RTT.

References

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