

**Symposium Title:** Modifying Quantitative Sensory Testing for intellectual and developmental disability populations: Promises and pitfalls

**Chair:** Frank Symons<sup>1</sup>

**Discussant:** James Bodfish<sup>2</sup>

**Overview:** The burden of pain among individuals living with severe (nonverbal, profound impairment) intellectual and developmental disabilities (IDD) is high. There are myriad reasons for this including frequent co-occurring medical conditions (e.g., chronic spasticity, scoliosis, intractable seizures), often necessitating invasive painful treatment (e.g., surgery, implants, orthotics) in the context of significant adaptive behavior constraints (e.g., communicative impairment) that can make it difficult to detect and recognize pain and therefore treat it. There has been over a decade's worth of work by different groups developing pain burden measurement approaches for individuals with severe developmental disabilities to accommodate the associated cognitive, motor, and communicative impairments. Although we have made progress towards agreement on what pain 'looks like' in nonverbal individuals with severe IDD (idiosyncrasies in expression notwithstanding), we are not necessarily closer to understanding 'what kind of pain'. It is well understood in the pain research community that not all pain is the same. One problematic unintended consequence of a singular focus on measuring and documenting pain burden is that it may be scientifically insufficient to lead to personalized pain treatment approaches because measures of pain burden are not necessarily designed to distinguish among pain mechanisms. Quantitative sensory testing (QST) is an approach used widely to evaluate chronic pain conditions among typically-developing adults and children that provides information about sensory gain and loss patterns that may be related to the pain mechanisms. Standard QST approaches are dependent on the ability of participants to respond verbally or behaviorally, and are likely confounded by motor delays. To overcome these issues, we have made adaptations to QST protocols to produce a modified quantitative sensory test (mQST) which can be applied in populations with motor and communicative impairments. The goal of this symposium is to review some of the populations in which this protocol has been applied to date and examine preliminary evidence of feasibility, utility, and validity. Dr. Frank Symons will begin the symposium with a brief overview of the history of the development of the mQST, and an overview of the current protocol.

## Paper 1 of 4

**Title:** Investigating the feasibility of a modified quantitative sensory testing approach to profile sensory function and predict pain outcomes following intrathecal baclofen implant surgery in cerebral palsy

**Authors:** Chantel C. Barney<sup>3</sup>, Alyssa M. Merbler<sup>1</sup>, Donald A. Simone<sup>1</sup> David Walk<sup>1</sup>, & Frank J. Symons<sup>1</sup>

**Introduction:** Chronic spasticity is often associated with pain in cerebral palsy (CP; Engel et al., 2003). Intrathecal baclofen (ITB) pumps used to manage spasticity in CP also improve pain outcomes for some but not all individuals with CP. The purpose of this clinical feasibility study was to explore whether a quantitative sensory testing approach could (a) be modified and used to subgroup individuals into sensory profiles and (b) test whether the profiles were related to post-implant pain outcomes (i.e., pain responsive or pain persistent).

**Method:** Participants were recruited from those scheduled to receive ITB pump implant surgery at a pediatric tertiary care hospital. A purposeful clinical sample of 9 children with CP (mean age = 12.5 years, male = 56%) and complex communication

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<sup>1</sup> University of Minnesota

<sup>2</sup> Vanderbilt University

<sup>3</sup> Gillette Children's Specialty Healthcare

needs participated. A prospective within-subject design was used to measure proxy-reported pain before and after ITB implant. Pain response status was determined by proxy-reported pain intensity change (> 50% change in maximum rated intensity). A modified quantitative sensory testing (mQST) procedure was used to assess behavioral responsiveness to an array of calibrated sensory (tactile/acute nociceptive) stimuli prior to surgery.

**Results:** Seven individuals with pre-surgical pain had mQST differentiated sensory profiles in relation to ITB pain outcomes and relative to the 2 individuals with no pain. Pre-surgically, the ITB pain-responsive subgroup (n=3, maximum rated pain intensity decreased >50% after ITB implant) showed increased behavioral reactivity to an acute nociceptive stimulus and cold stimulus whereas the ITB pain persistent subgroup (n=4) showed reduced behavioral reactivity to cold and repeated von Frey stimulation relative to the no pain individuals.

**Discussion:** These results indicate a quantitative sensory testing approach is feasible for a sample of children with CP undergoing ITB pump implant surgery. We found that ITB pain responders showed more behavioral reactivity pre-ITB implant, while ITB pain non-responders showed less reactivity to the sensory stimuli. Implications for patient selection criteria and stratification to pre-surgically identify individuals with CP 'at risk' for persistent post-procedure pain will be discussed.

#### References/Citations:

- Engel JM, Jensen MP, Hoffman AJ et al. Pain in persons with cerebral palsy: Extension and cross validation. Arch Phys Med Rehabil 2003; 84: 1125-8.

#### Paper 2 of 4

**Paper Title:** Behavioral Reactivity during a Modified Quantitative Sensory Test in Rett Syndrome

**Authors:** Alyssa Merbler<sup>1</sup>, Breanne Byiers<sup>1</sup>, Chantel Barney<sup>3</sup>, & Frank Symons<sup>1</sup>

**Introduction:** Rett syndrome is a severe neurodevelopmental disorder, most often caused by a mutation in the methyl-CpG-binding protein 2 (MECP2) gene.<sup>1</sup> MeCP2 may be involved in sensory and nociceptive processes, and thus there may be alterations in pain perception/experiences in this population.<sup>2</sup> Some descriptions of RTT have included decreased or absent pain response, while others have documented responses to painful stimuli.<sup>3</sup> Traditional pain and sensory assessment is difficult, if not impossible, in this population, due to motor and communication impairment. The purpose of this study was to measure non-verbal behavioral reactivity (BR) during a modified quantitative sensory test (mQST) to describe sensory profiles in a small sample of individuals with RTT.

**Methods:** Twenty-two girls and women with Rett were included in this sample (mean age = 17 years, range = 2-52 years). We conducted the mQST on both hands and feet. Nine participants had a repeated mQST several months to a year later. Pain- and discomfort-related BR, as used previously in this population,<sup>4</sup> was coded during each stimulus. This included vocal (e.g. crying), facial, body, and physiological behaviors.

**Results:** There was extreme variability in BR overall, with some individuals showing very low levels of BR (or even no BR during some stimuli), to others terminating specific stimuli due to extreme reactivity. Cronbach's alpha was .87 for BR scores of all stimuli. Repeated von Frey showed the highest predicted values, followed by cool, pressure, heat, pin, light touch, and sham. Pairwise comparisons show cool, pressure, repeated von Frey, and heat were significantly different than sham scores. There was a significant main effect of stimulus, age, and clinical severity on BR scores of the stimuli compared to sham, and a significant clinical severity by stimulus interaction for pressure and heat. For those with two administrations, total scores were stable across time (ICC=.7).

**Discussion:** The results demonstrate that the individuals in this sample did perceive and respond to different tactile stimuli of the mQST, indicating that the mQST may be a useful tool to investigate sensory function in this population. These findings replicate some of the findings of a preliminary study of this mQST in RTT,<sup>4</sup> however some specifics of the patterns across stimuli differ. The

mQST also seems to be measuring a relatively stable construct in this sample, as total BR scores of two mQSTs months apart were stable. Continuing challenges and areas for future research include ensuring the BR coding system that captures a range of behavioral reactivity profiles, finding an application site that balances feasibility with scientific integrity (e.g. limiting participant view of the stimulus application), and implementation and analytical considerations related to potential delayed responding to stimuli.

**References/Citations:**

1. Amir, R. E., Van den Veyver, I. B., Wan, M., Tran, C. Q., Francke, U., & Zoghbi, H. Y. (1999). Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. *Nature Genetics*, 23(2), 185.
2. Martin, P. (2017). Pain in Rett syndrome: peculiarities in pain processing and expression, liability to pain causing disorders and diseases, and specific aspects of pain assessment. *Advances in Autism*, 3(3), 163-182.
3. O'Leary, H. M., Marschik, P. B., Khwaja, O. S., Ho, E., Barnes, K. V., Clarkson, T. W., ... & Kaufmann, W. E. (2017). Detecting autonomic response to pain in Rett syndrome. *Developmental Neurorehabilitation*, 20(2), 108-114.
4. Merbler, A. M., Byiers, B. J., Hoch, J., Dimian, A. C., Barney, C. C., Feyma, T. J., ... & Symons, F. J. (2019). Preliminary Evidence That Resting State Heart Rate Variability Predicts Reactivity to Tactile Stimuli in Rett Syndrome. *Journal of Child Neurology*.

**Paper 3 of 4**

**Paper Title:** Assessing Sensory Perception and the Behavioral Function of SIB

**Authors:** Griffin W. Rooker<sup>4,5</sup>, Louis P. Hagopian<sup>4,5</sup>, Frank J. Symons<sup>1</sup>, Erica Lozy<sup>5</sup>, Alyssa M. Merbler<sup>1</sup>, Christopher Dillon<sup>5</sup>, & Drew Piersma<sup>5</sup>

**Introduction:** Some individuals with intellectual and developmental disabilities are reported to engage in self-injurious behavior (SIB). These behaviors pose a significant risk to health and safety, leading to increased hospitalization and profoundly influencing quality of life. Both biological and environmental variables are relevant in the occurrence of SIB. In particular, both sensory perception and function of the behavior have been implicated in the occurrence of this behavior.

**Methods:** To assess the interaction of these variables, we conducted a functional analysis (to determine the function of behavior) and modified quantitative sensory testing (MQST) on a sample of 16 individuals who engaged in SIB (SIB group). In addition, we conducted this MQST on five individuals not reported to engage in SIB (no SIB group).

**Results:** Results are preliminary, but suggest that individuals who engage in SIB were more reactive to sensory stimulation. Further individuals with one particular subtype of SIB (automatically reinforced subtype-2 SIB) were the most sensitive to sensory stimulation and the greatest magnitude of difference appeared with deep pressure stimulation.

**Discussion:** These results replicate some sensory finding in the literature (Symons et al., 2010) and align with differences observed in injury profiles across different function of SIB (Rooker et al., in press).

**References/Citations:**

- Rooker, G.W., Hagopian, L.P., Becraft, J.L., Javed, N., Fisher, A.B., & Finney, K.S. (in press). Injury Characteristics Across Functional Classes of Self-Injurious Behavior. *Journal of Applied Behavior Analysis*.
- Symons, F. J., Harper, V., Shinde, S. K., Clary, J., & Bodfish, J. W. (2010). Evaluating a sham-controlled sensory-testing protocol for nonverbal adults with neurodevelopmental disorders: self-injury and gender effects. *The Journal of Pain*, 11, 773-781.

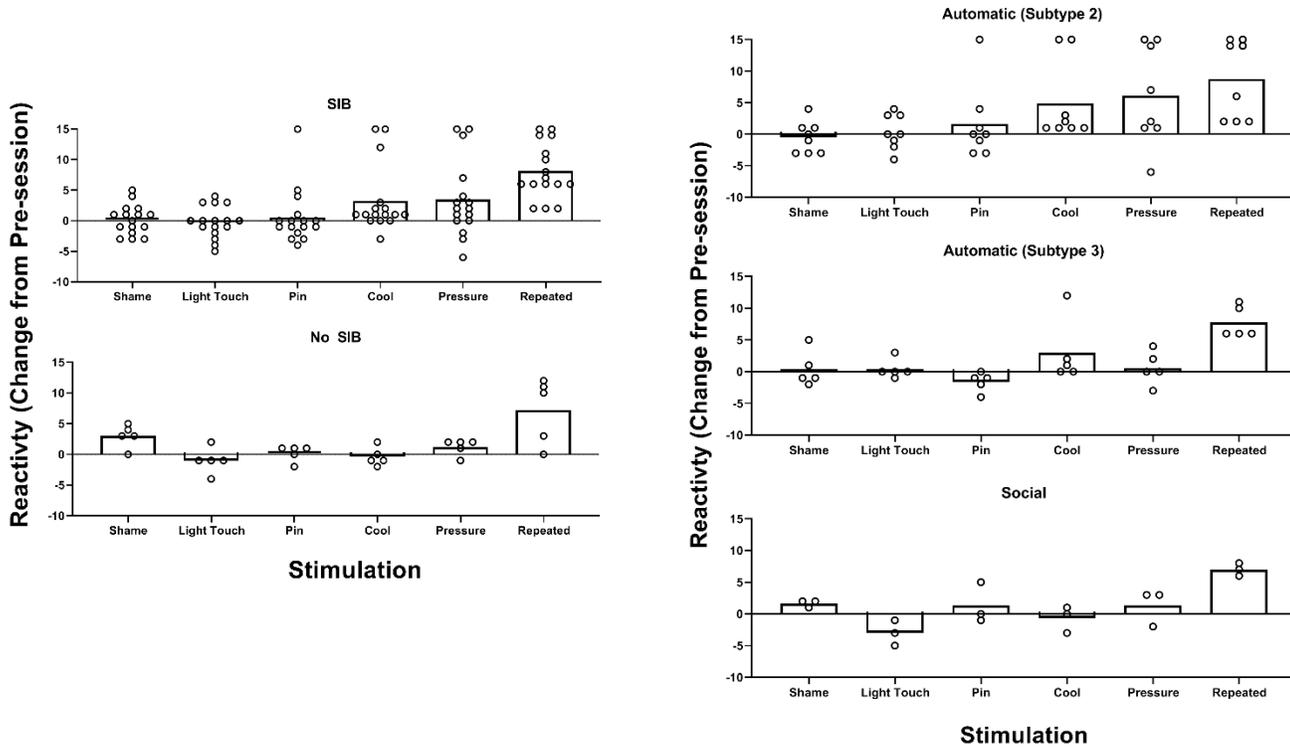
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<sup>4</sup> Johns Hopkins University School of Medicine

<sup>5</sup> Kennedy Krieger Institute

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Representative graphs: Left figure: Change in reactivity across SIB and no SIB groups. Right Figure Change in reactivity across different SIB groups (based on function).



Paper 4 of 4

**Paper Title:** Evaluation of the mQST in a typically-developing comparison group

**Authors:** Breanne Byiers<sup>1</sup>, Alyssa Merbler<sup>1</sup>, Chantel Barney<sup>3</sup>, Frank Symons<sup>1</sup>

**Introduction:** Although the mQST was developed specifically for use with individuals with intellectual and developmental disabilities (IDD), it is important to understand how well it functions as an assessment across a broad range of populations. The goal of this study was to evaluate how typically-developing children and adults respond to the mQST protocol at the level of self-reported experience, behavioral reactivity, and physiological reactivity.

**Methods:** A total of 44 individuals aged 1.5 to 39 years of age (52% male) participated in the study. In addition to completing the mQST, participants provided saliva samples at multiple points throughout the study visit to evaluate changes in stress-related hormones (i.e., cortisol, salivary alpha-amylase, and beta-endorphin), and wore heart rate and respiration monitoring equipment throughout the visit. Reactivity during the mQST was evaluated using self-reported experience (0-10 rating scales for “bothersomeness” and yes/no responses in response to “Did you feel that?” and “Did it hurt?” for each stimulus), and automated facial action coding.

**Results:** 38 participants were able to provide verbal self-report. The repeated mechanical stimulus was most likely to be reported as painful (57%), and was also associated with the highest “bothersomeness” score (min = 1, max = 10, mean = 4.5), followed by pin prick, with 50% of participants reporting that it hurt, and a mean bothersomeness rating of 3.6 (min = 0, max = 10). No

participants reported the sham or light touch stimuli as painful, and only one (3%) reported the cool stimulus as painful. Preliminary analyses suggest that younger participants reported higher scores for most stimuli, and that this age effect was stronger in males than in females. Preliminary examination of heart rate and heart rate variability changes in response to each stimulus application showed decreases in heart rate and increases in heart rate variability during stimulus applications compared to inter-stimulus intervals, a pattern commonly seen in orienting or attentional responses, but these changes did not differ across stimuli. Analysis of behavioral reactivity and salivary biomarkers is ongoing.

**Discussion:** These results show that there is a wide range of responses to the mQST protocol, even among typically-developing children and adults. As expected, most participants rating the stimuli as no more than mildly painful, but there was a wide range of “bothersomeness” ratings for many of the stimuli, suggesting that they are sufficiently intense to provoke behavioral responses. Preliminary evidence from changes in heart rate suggest that physiological measures may be a useful addition to behavioral responding in evaluating subjective experience during the mQST. Results will be discussed in relation to difficulties in comparing across IDD and non-IDD diagnostic groups due to possible motor and cognitive confounds.