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Pain experience and expression in Rett syndrome: Subjective and objective measurement approaches

Chantel C. Barney, Ph.D.[1,2], **Timothy Feyma, M.D.**[1], **Arthur Beisang, M.D.**[1], and **Frank J. Symons, Ph.D.**[2]

[1]Gillette Children's Specialty Healthcare, 200 University Ave, Saint Paul, MN 55101

[2]Department of Educational Psychology, University of Minnesota, 56 East River Road, Minneapolis, MN 55455

Abstract

Rett syndrome (RTT) is associated with myriad debilitating health issues and significant motor and communicative impairments. Because of the former there is concern about the possibility of recurrent and chronic pain but because of the latter it remains difficult to determine what pain 'looks like' in RTT. This study investigated pain experience and expression using multiple complementary subjective and objective approaches among a clinical RTT sample. Following informed consent, 18 participants (all female) with RTT (mean age= 12.8 years, SD= 6.32) were characterized in terms of pain experience and interference, typical pain expression, and elicited pain behavior during a passive range of motion-like examination procedure. Parents completed the Dalhousie Pain Interview (DPI; pain type, frequency, duration, intensity), the Brief Pain Inventory (BPI; pain interference), and the Non-Communicating Children's Pain Checklist – Revised (NCCPC-R; typical pain expression). A Pain Examination Procedure (PEP) was conducted and scored using the Pain and Discomfort Scale (PADS). The majority of the sample (89%) were reported to experience pain in the previous week which presented as gastrointestinal (n=8), musculoskeletal (n=5), and seizure related pain (n=5) that was intense (scored 0–10; *M*= 5.67, *SD*= 3.09) and long in duration (*M*= 25.22 hours, *SD*= 53.52). Numerous pain-expressive behaviors were inventoried (e.g., vocal, facial, mood/interaction changes) when parents reported their child's typical pain behaviors and based on independent direct observation during a reliably coded pain exam. This study provides subjective and objective evidence that individuals with RTT experience recurring and chronic pain for which pain expression appears intact.

Keywords

Rett syndrome; neurodevelopmental disability; MeCP2; pain; measurement

Correspondence should be addressed to Chantel Barney, Gillette Children's Specialty Healthcare, 200 University Ave, Saint Paul, MN 55101, Fax: 651-229-1767, cbarney@gillettechildrens.com.

Ethical approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Rett syndrome (RTT) is a severe neurodevelopmental disorder predominantly affecting females and is caused primarily by mutations in the methyl-CpG-binding protein 2 gene (*MECP2*). It is characterized by apparently normal pre- and perinatal development, normal head circumference at birth, deceleration of head growth between 5 months and 4 years of age, loss of acquired purposeful hand skills followed by the development of stereotypical hand movements, as well as severe impairments in expressive and receptive language, and gait apraxia (Neul, et al., 2010). There are numerous chronic health and behavior problems associated with RTT for which it would be reasonable to expect pain or discomfort (e.g. scoliosis, constipation and related gastrointestinal problems, self-injurious behavior).Yet there also seems to be an apparent pain insensitivity or indifference reported by providers and caregivers (Downs, et al., 2010; Hagberg et al. 2001; Hagberg 2002), although there is some evidence of non-verbal pain expression consistent with other neurodevelopmental disorders (Symons et al. 2013). Overall, the scientific literature specific to pain in RTT is limited and a fair conclusion is that pain is not well understood or documented in detail in RTT.

Given the nature of the syndrome and its underlying pathophysiology, it is reasonable to wonder whether the mechanisms supporting nociceptive signaling are intact. MeCP2 is a critical protein for neuronal development; the loss of which leads to profound neuronal dysfunction and abnormal brain development. The available evidence from preclinical investigations suggests that reflexive pain circuitry is intact but that high-order discriminatory behavior may be impaired (Samaco et al. 2008; note, however, that there may be motor confounds in the reported behavioral assays making the interpretation of withdrawal latencies and related metrics difficult to interpret). Of relevance to nociceptive signaling pathways, MeCP2 is also localized in the dorsal horn, specifically in neurons, oligodendrocytes and astrocytes with evidence of opposite effects depending on inflammatory (upregulation) or neuropathic (down regulation) pain models. There is also evidence that MeCP2 is important for mu opioid receptor regulation (Hwang et al. 2009). Taken together, it does seem that through epigenetic mechanisms, MeCP2 plays an important role in the development and function of highly relevant components of the nociceptive circuitry, but the relation between the pre-clinical models and the clinical pain phenotype is not well established.

In prior clinical and clinically-relevant work there have been three studies in which pain was explicitly measured. One was a case report documenting reduced post-operative analgesic requirements following surgical intervention for scoliosis (Konen et al. 1999). This case study included direct behavioral ratings and maternal report and suggested reduced pain (expression). Similarly, in a large caregiver survey (N = 646) based on multi-national registries that included an item or items about altered pain sensitivity the majority of parents reported reduced pain sensitivity with the effect most pronounced among younger cases, although when severity of impairment/disability was controlled for the effects were marginal (Downs et al. 2010). For some cases, pain sensitivity was reported as increased. There appeared to be a distinction between “external” pain (their term; from trauma, falls, accidents, etc.) as being reduced but “internal” pain (again, their term, from gastrointestinal, etc.) as being increased. There was also preliminary evidence that genotype mattered with a

C-terminal, p.R168X or p.R306C mutation associated with decreased pain sensitivity. In a smaller survey but with more specific pain measures it was reported that 24% of parents (out of 44) responded that their daughters experienced pain cumulatively for more than 1 week in the previous 30 days (Symons et al. 2013). Pain frequency was significantly correlated with age, number of pain sources and the number of known health problems; the number of pain sources was significantly correlated with number of health problems as well. An equally important and perhaps more troubling finding, however, was that 43% of parents reported they were unsure how to tell whether there daughter was in pain. Ninety percent of the individuals reported on in the sample with RTT were nonverbal. Clearly there is a need to develop new approaches for evaluating pain in RTT or, alternatively, to apply existing approaches that have been developed for use with non-verbal individuals with neurodevelopmental disabilities.

Using the latter strategy, the purpose of this descriptive study was to examine in more detail pain experience and expression in RTT. The specific objectives were to 1) generate qualitative and quantitative inventories about proxy-reported pain experience (type, duration, intensity) by directly interviewing primary caregivers (parents, guardians) about their daughter with RTT; 2) document the extent to which any reported pain interfered with activities of daily living (ADL); and 3) apply an existing exam-based pain assessment protocol (described below) to catalog reliably observable behavior consistent with pain expression.

Materials and Methods

Participants

Appropriate ethical approval was obtained for this study and informed consent was obtained on behalf of all individuals included in the study. A consecutively enrolled convenience sample of 18 girls and women living with RTT (mean age= 12.8 years; SD= 6.32; range = 4–29; 100% Caucasian) were recruited. All participants were nonverbal. More than half (55.6%) of participants had at least one chronic health condition that parents reported to be painful. These conditions included hip dislocation/subluxation (n=6), gastrointestinal complications (e.g., gas, bloating, constipation; n=4), scoliosis (n=2), seizures (n=1), and undiagnosed ongoing pain (n=1).

Procedures

Each participant was characterized in terms of pain experience and interference, typical pain expression, and any pain expression elicited during a physical exam. Each participant was tested individually in a clinic or family consultation room. The parents were given instructions and asked to complete the Non-Communicating Children’s Pain Checklist – Revised (NCCPCR) and the Brief Pain Inventory (BPI) on their own during the assessment time. The physical exam was conducted with the participant either seated in their wheelchair or seated on a chair with a video camera positioned approximately three meters away and orthogonal to the participant. The Dalhousie Pain Interview (DPI) was then conducted afterward in an interview format with the parent(s) or caregiver(s).

Measures

Direct Physical Exam—The Pain Examination Procedure/Pain and Discomfort Scale (PADS/PEP; Bodfish et al. 2006; Phan et al. 2005) was used to measure pain expression. The PADS/PEP approach is unique in that it measures pain expression during a short standardized passive range-of-motion like pain examination procedure (PEP) providing the assessor the possibility of isolating a pain source/location. The PADS was derived from the Non-Communicating Children's Pain Checklist – Revised (NCCPC-R; Breau et al. 2002). Each of 18 items on the PADS was scored from 0–4 with 0 meaning the behavior was never observed to 4 meaning the behavior was observed continuously throughout the observation period. The PADS/PEP approach has been used in prior pain research with non-verbal individuals with developmental disabilities (Phan et al. 2005). The observation and scoring system has been reported on with high levels of inter-observer agreement (ranging from 93–100%), reliability evidence, and validity evidence.[9] The inter-observer agreement for this sample was 96.2% (92.2–98.9%).

Parent Questionnaires—The Brief Pain Inventory (BPI; Tyler et al. 2002) was used to measure the extent to which pain interfered with twelve different aspects of daily living including communication, mobility, school, daily activities, self-care, sleep, and mood in the previous week. The BPI has been used with other non-verbal samples of individuals with developmental disabilities and produced reliable scores (Barney et al. 2013; Osborne et al. 2006). In this sample the BPI had excellent internal consistency (.97) and significantly correlated with parent reported pain expression ($r=.58$, $p=.01$) and pain frequency ($r=.49$, $p<.05$) providing evidence for its concurrent validity as applied in this study.

The Dalhousie Pain Interview (DPI; Breau et al. 2003) was based on parent/guardian proxy-report and used to generate subjective evidence specific to the nature of the pain experience. The DPI is a 10 item structured interview from which the type, frequency, duration, and intensity of pain experienced in the previous week was derived. Specific items are anchored to whether there has been pain in the past week, its general description, possible cause, duration (cumulative hours, minutes, and seconds), frequency (number of episodes), and intensity (0–10; zero means "no pain at all" and ten means the "worst pain ever"). All pain episodes reported are categorized as accidental, gastrointestinal, musculoskeletal, neurological, stretching, positioning, equipment, orthopedic, spasm, other, or unknown pain. Up to two pain relieving treatments are documented (if applicable) for each type of pain described. Parents/guardians are asked to report how effective the treatment was for relieving the pain from 0 "it didn't help at all" to 10 "it completely relieved the pain". The DPI has been used in previous studies with individuals with developmental disabilities (Barney et al. 2013; Breau et al. 2001).

The Non-Communicating Children's Pain Checklist - Revised (NCCPC-R; Breau et al. 2002) is an observational assessment scale that was used to quantify parent's report of the typical signs of pain they observe when their child experiences pain. The NCCPC-R has been used in many applications with non-verbal or otherwise communicatively-impaired individuals with significant developmental disabilities and has demonstrated strong inter-rater reliability and internal consistency (Belew et al. 2013; Breau et al. 2001; Breau et al.

2002; Breau et al. 2003). In this sample the NCCPC-R had excellent internal consistency (. 91) as applied in this study.

Results

1) Proxy-reported pain expression and experience (type, duration, intensity)

The majority of the sample (n=16/18; 89%) were reported to have experienced pain in the previous week and ~38% (n=6) of those experienced more than one type of pain. Pain presented as gastrointestinal (n=8), musculoskeletal (n=5), seizure related pain (n=5), accidental/every day pain (n=3), other (dental pain; n=1), and unknown (n=1). On average, with all pain types combined, the pain reported was intense (scored 0–10; *M*= 5.67, *SD*= 3.09), long in duration (*M*= 25.22 hours, *SD*= 53.52) and frequent (M= 3.16 episodes, SD= 2.80; see Table 1 for pain duration, intensity and frequency of episodes by pain type). When considering only the most severe pain reported for each participant in the previous week (intensity M=6.75, SD=1.98, range= 3–10/10; duration M=37.15 hours, SD=56.31, range= 5 min - constant), 94% of participants experienced pain of significant intensity (≥4/10) typically considered to warrant pharmacological intervention. Only 27% received a pharmacological treatment for their most severe pain. However, many parents reported taking some action to alleviate their child's pain in the previous week (66.7%) and 28% reported attempting more than one type of pain relief method. Medication, massage, and distraction were the most frequent treatments used in the previous week (Table 2). Parent report of their daughter's typical pain expression (NCCPC-R) covered a wide range of non-verbal pain signs. Rather than reduce what is arguably ordinal data to simple means, the cumulative endorsement of NCCPC-R pain items are presented in Table 3.

2) Proxy-reported pain interference with activities of daily living (ADL)

The majority of the sample experienced pain that interfered to some extent with activities of daily living in the previous week (n=15; 83%). The BPI mean total score for this sample was 34.33 (scored 0–120; SD=26.96) and individual total scores ranged from 0 (n=2; pain did not interfere at all with ADL) to 120 (n=1; pain interfered completely with all ADL). Parents reported that pain most interfered with their daughter's mood (scored 0–10; M=4.00, SD=2.33), social interactions (M=3.39, SD=2.99), communication (M=3.11, SD=2.81), and mobility (M=3.11, 3.12) in the previous 7 days.

3) Objective (PADS/PEP) characterized pain expression

The majority of the sample (n=15; 83%) exhibited pain-expressive behaviors during the PEP. The PADS mean total score for this sample was 10.67 (scored 0–72; SD= 10.86) and individual scores ranged from 0 to 41. Multiple pain-expressive behaviors occurred frequently and were directly observed and quantified including facial expressions (e.g., grimace, furrowed brow, change in eyes; M=5.78, SD=5.41), vocal expressions (e.g., moaning, crying, screaming; M=1.89, SD=4.61), mood/interaction expressions (e.g., not cooperating, resists interaction; M=1.39, SD=4.03), and body and limb expressions (e.g., favors body part, flinches; M=1.61, SD=3.96). There were no occurrences observed of 'physiological expressions' of pain (e.g., tears, sharp intake of breath, breath holding, noisy

breathing; M=0.00, SD=0.00). Pain behavior was observed while the examiner manipulated the head (M=1.78, SD=2.37), arms (M=5.11, SD=7.07), and legs (M=3.72, SD=3.59).

4) Concordance between proxy reported pain behavior (i.e., subjectively estimated) and directly observed pain behavior (expressed, i.e., objectively estimated)

Proxy reported pain interference (total BPI score) correlated with proxy reported pain expression (NCCPC-R total score; r=.58, p=.01) and pain frequency (DPI; r=.49, p<.05). Pain expression observed during the standardized pain exam (PEP) and scored objectively (PADS) did not significantly correlate with subjective proxy reported measures of pain intensity (r=.28, p=.27), duration (r=.21, p=.41), frequency (r=.01, p=.97), BPI total score (r= −.06, p=.80), or NCCPC-R total score (r=.30, p=.23).

Discussion

The results from this study suggest that pain was a problem for a significant subgroup of girls and women living with RTT – with 89% of the sample experiencing some form of reported pain in the prior week, the majority of whom (94%) experienced pain severe enough to warrant pharmacological intervention. On average, 37 hours of severe pain (scored 7 out of 10) was reported in the previous week. Not surprisingly, pain impacted activities of daily living. Data in Table 4 provides comparison with other samples with intellectual and developmental disabilities for which the same measures have been used. Reported pain prevalence in this sample of girls and women with RTT appeared comparable to the high pain prevalence reported in children with cerebral palsy. On one hand this is not surprising given both groups experience a myriad of chronic conditions (i.e., spasticity, constipation, muscle spasms) secondary to their diagnosis, but on the other hand this is noteworthy because pain is now more readily acknowledged in cerebral palsy (Barney et al. 2013; Ramstad et al. 2011) whereas girls and women with RTT are often suspected to be less sensitive or insensitive to pain (Downs et al. 2010; Hagberg 2002; Konen et al. 1999). Pain intensity and frequency were comparable across groups, supporting the concern that pain is a problem for individuals with intellectual and developmental disabilities in general. Duration of reported pain was greater for the current RTT sample and pain interfered to a greater extent with activities of daily living. Additionally, observed pain behaviors during the PEP for the RTT sample appeared comparable to observed pain behaviors from a group of individuals with IDD experiencing a painful dental scaling procedure.

There were statistically significant correlations among the subjective (proxy-reported) variables. The correlations between the subjective and objective measures were not significant. This might not be unexpected given the complexity of the pain construct. Assessing another's pain is a difficult task even when cognitive and communicative abilities are intact (Hadjistavropoulos and Craig 2002; Schiavenato and Craig 2010). In a previous study of parent-reported pain in RTT, 43% of parents were unsure how to tell when their daughter was in pain (Symons et al. 2013). Other studies have also found that parents have more difficulty estimating pain when their child has an intellectual or developmental disability (Nader et al. 2004). One study found that parents were unable to detect dental pain in their child until there were obvious physical signs present (e.g., swelling, redness)

suggesting parents may under report their child's pain (Hennequin et al. 2000). Additionally, it should be noted that parents were asked to recall their daughter's pain history over the previous 7 days, whereas the pain exam was conducted at the time of study participation. The disparity in sampling time frame, as well as the small sample size, may have also contributed to the non-significant correlations. Descriptively, however, both objective and subjective measures were indicative of high levels of pain behavior (either in the prior week or upon exam) in this sample. The finding highlights the need for multiple methods of assessment in communicatively complex individuals.

Among the pain sources visceral and musculoskeletal pain were frequently reported. This finding is consistent with Down et al.'s large RTTNET survey in which parents made a distinction between 'external' and 'internal' pain to the degree that 'external pain' may be analogous to 'acute nociceptive pain' and 'internal pain' analogous to 'visceral pain' (Downs et al. 2010). Although the mechanisms regulating visceral pain are less well understood than nociceptive pain (Christianson & Davis 2010), converging behavioral pain phenotype findings as discussed above suggest that visceral pain may well be an important clinical problem in RTT and in need of further scientific investigation. From a clinical care perspective, the frequent health issues and communication impairments associated with RTT suggest that girls and women living with RTT may be at an increased risk for pain to be overlooked or discounted. Our findings suggest careful evaluation using non-verbal rating scales or standardized exam can reveal evidence for intact pain signaling.

In terms of pain neurobiology and the biology of RTT, there may be a complex interaction between nociceptive and inflammatory mechanisms related to untreated pain, its chronicity, and the possibility of activated 'central sensitization' mechanisms contributing to the RTT behavioral phenotype. It has been shown that MeCP2 is phosphorylated in lamina I projection neurons following the induction of peripheral inflammation (Geranton et al. 2007). Lamina I neurons are implicated in the development of pain states (Khasabov et al. 2002), and thus there is the possibility that MeCP2 also contributes to chronic inflammatory pain states. This suggestion is speculative, however, and the evidence generated by our study is not confirmatory of such a relationship.

There have been claims that RTT is associated with elevated pain thresholds (Devarakonda et al. 2009). The evidence reported here does not directly address that issue (i.e., this was not a threshold study) but it does provide additional subjective and objective evidence that girls and women living with RTT are reported to experience recurring and chronic pain for which pain expression appears to be intact. Reconciling our findings with the notion of 'elevated thresholds' is not necessarily warranted. It is worth commenting, though, that the notion of 'elevated thresholds' may be an artifact of the extreme motor impairment associated with the disorder (i.e., failure to react time-dependently to noxious stimuli is taken as prima facie evidence for elevated pain threshold but it may be, at least in part, an artifact of functional motor impairment). Work designed to examine and establish sensory and nociceptive thresholds in this population will need to attend to the presence of impaired motor control. It is also worth noting that how the questions are asked (e.g., open ended questionnaires, standardized pain inventories, etc.) may well determine what gets found with respect to caregiver impressions about their daughter's pain experience and expression.

One problem with the approach we used is there may be some confusion about what is assumed with respect to the 'pain examination procedure' (the PEP). The name implies that pain is being examined; therefore one assumption is that pain must be present or the corollary – any behavior observed during the PEP 'must' be pain. Both these options are unknowable in the absence of self-report. The purpose of the exam-based approach however was to (a) introduce some degree of standardization (i.e., all participants were evaluated in the same way) and (b) use directly observable behavior time-locked to the exam as one indicator of a behavioral response. In terms of limitations, then, it is clear that we have no independent verification of pain. That issue was, in part, the reason for the study – to compare subjective and objective evaluations of pain/pain behavior in RTT to test whether they may at least be concordant. While correlations between subjective and objective variables were not statistically significant they were concordant as both demonstrated high levels of pain/discomfort in this sample.

Overall, it would appear that in this sample of individuals with RTT, there were concerns about chronic pain experience associated with visceral and related pain, the behavioral capacity for pain expression was intact, and that pain interfered with activities of daily living. The current sample was too small to examine genotype/mutation differences in relation to pain profiles but that idea warrants further investigation given Down et al.'s prior large survey (Downs et al. 2010). Finally, much more work is needed to understand the biology of RTT with respect to MeCP2 protein function and, in particular, dorsal horn physiology and nociceptive signaling. Such mechanisms oriented investigations are needed if we are to establish evidence-based practice and clarify standard of care issues with respect to opioid use and analgesic management. Work coming 'up' from the RTT genotype and 'down' from the phenotype informing one another would be optimal to understand pain in this clinically difficult and vulnerable population.

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Table 1

Proxy reported pain duration, intensity, and frequency of episodes by pain type in the previous 7 days.

Pain Type	Number of Participants (n=)	Median Duration	Mean Duration (SD; range)	Median Intensity	Mean Intensity (SD; range)	Median Episodes	Mean Episodes (SD; range)	Medication Administered (n=)
Gastrointestinal	8	13.50	24.85(27.53; 0.33–72)	6	5.88 (2.17); 3–9	2.5	3.87(4.26; 1–14)	4
Musculoskeletal	5	84.00	84.07(83.91; 0.11–168)	6	6.60 (1.82); 5–9	1	2.60(2.61; 1–7)	2
Seizure related	5	3.00	9.70(12.16; 0.5–30)	5	5.50 (2.52); 3–9	1	5.20(8.32; 1–20)	3
Everyday	2	0.13	0.13(0.16; 0.02–0.25)	4	4.00 (4.24); 1–7	1	1.00(0.00; 1–1)	0

Pain duration reported in hours. Pain intensity scored 0–10.

Table 2

Pain relief methods and associated proxy reported therapeutic effect

Pain Relief Method	Number of Participants (n=)	Median Treatment Efficacy	Mean Treatment Efficacy (SD; range)	Pain Type Treated (n=)
Medication	8	6	6.43 (2.16; 3–10)	Gastro (4)/ Seizure (3)/ Musc (1)
Massage	6	5.5	5.75 (1.75; 0–6)	Gastro (3)/Musc (1)/Everyday (2)
Distraction	4	4	3.50 (1.67; 3–9)	Seizure (3)/Musc (1)

Treatment efficacy scored 0–10. Gastro = Gastrointestinal pain, Seizure = seizure related pain, Musc = Musculoskeletal pain, Everyday = Everyday pain

Table 3

Parental endorsement of Non-Communicating Children's Pain Checklist-Revised (NCCPC-R) items when asked to recall typical pain expressions exhibited by their daughter (n=18).

NCCPC-R item:	0 = not at all (n=)	1= Just a little (n=)	2= Fairly Often (n=)	3 = Very often (n=)
Vocal				
Moaning, whining, whimpering (fairly soft)	1	7	4	6
Crying (moderately loud)	4	3	7	4
Screaming/yelling (very loud)	8	3	4	3
A specific sound or word for pain (e.g., a word, cry or type of laugh)	9	4	3	2
Social				
Not cooperating, cranky, irritable, unhappy	0	6	7	5
Less interaction with others, withdrawn	7	4	4	3
Seeking comfort or physical closeness	5	4	3	6
Being difficult to distract, not able to satisfy or pacify	3	7	4	4
Facial				
A furrowed brow	4	6	6	2
A change in eyes including: squinching, eyes opened wide, eyes frowning	3	5	6	4
Turning down of mouth, not smiling	3	7	5	3
Lips puckering up, tight, pouting, or quivering	6	7	2	3
Clenching or grinding teeth, chewing or thrusting tongue out	4	4	2	8
Activity				
Not moving, less active, quiet	3	11	0	4
Jumping around, agitated, fidgety	10	1	4	3
Body and Limbs				
Floppy	12	4	1	1
Stiff, spastic, tense, rigid	2	4	5	7
Gesturing to or touching part of the body that hurts	13	3	1	1
Protecting, favoring or guarding part of the body that hurts	11	3	4	0
Flinching or moving the body part away, being sensitive to touch	7	6	3	2
Moving the body in a specific way to show pain (e.g., head back, arms down, curls up, etc.)	5	6	5	2
Physiological				
Shivering	11	5	2	0
Change in color, pallor	8	3	7	0
Sweating, perspiring	11	4	2	1
Tears	3	5	6	4
Sharp intake of breath, gasping	3	6	6	3
Breath holding	5	8	1	4
Eating/Sleeping				
Eating less, not interested in food	9	3	1	5
Increase in sleep	11	3	1	3

NCCPC-R item:	0 = not at all (n=)	1= Just a little (n=)	2= Fairly Often (n=)	3 = Very often (n=)
Decrease in sleep	10	1	2	5

Table 4

Pain parameters in girls and women with RTT compared to other study samples with intellectual and developmental disabilities using the same pain measures.

	Rett Syndrome (Current study) n=18	Intellectual Disability (Breau et al., 2003) n=94	Cerebral Palsy (Barney, et al., 2013) n=34	Intellectual Disability (Phan et al., 2005) n=28
Proportion with pain	16 (89%)	33–49 (35–52%)	32 (94.1%)	-
Intensity (0–10)	5.67 (3.09)	Accidental 3.8 (2.1) Non-accidental 6.1 (2.2)	4.48 (1.77)	-
Frequency (episodes)	3.16 (2.80)	1.08	7.64 (7.13)	-
Duration (hours)	25.22 (53.52)	~9	2.64 (4.27)	-
BPI (total score)	34.33 (26.96) range 0–120	-	13.09 (21.22) range= 0–82	-
PADS (total score)	10.67 (10.86) range= 0–41	-	10.50 (10.67) range= 0–34	6.04

BPI=Brief Pain Inventory (pain interference with activities of daily living), PADS= Pain and Discomfort Scale (observational measure of pain during physical exam)