

# **Understanding Chronic Pain in Individuals with Autism Spectrum Disorders**

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# OVERVIEW

- **DEVELOPMENT OF CHRONIC PAIN**
- **ASSESSING PAIN IN INDIVIDUALS WITH ASD**
- **POSSIBLE REASONS FOR PAIN IN INDIVIDUALS WITH ASD**
- **EVALUATION AND TREATMENT IMPLICATIONS**

# Chronic Pain

- **Continued visceral or somatic sensory central nervous system noxious input related to injury, infection, metabolic disease, inflammation, or structural changes (e.g bowel obstruction)**
- **Dysregulated integration of pain transmission and inhibitory systems (e.g. irritable bowel disorder: neuroenteric dysregulation)**

# Pain Assessment

- **Verbal: pain ratings, descriptors**
- **Behavior:**
  - **Crying**
  - **Withdrawal**
  - **Avoidance of movement**
  - **Protection of a body part**
  - **Irritability**

# Pain Assessment

- **Physiologic:**
  - **Tachycardia**
  - **Increased BP**
  - **High stress hormones**
  - **Increased beta endorphin**

# Pain Assessment

- **Chronic pain responses can be different from acute pain responses:  
e.g. flat cortisol response**

# Pain Assessment in ASD

- **Difficulties in communication**
- **Narrowed focus of interest (which may become the pain)**
- **Limited array of self-soothing or means of coping with pain**

# Pain Assessment in ASD

- **May respond to stress with self-injurious or aggressive behaviors**
- **May have co-morbid anxiety**
- **Difficulties filtering sensory stimuli, increasing overall arousal and making pain worse.**



# Pain Assessment in ASD

- **Communication about the personal experience of chronic pain is complicated and difficult in ASD**
- **Interpreting pain behavior in ASD is complicated, since the setting/environment can influence pain behaviors which can be more global or stereotypic than pain specific**

# Pain Assessment in ASD

- **Are there inherent differences in pain sensitivity in individuals with ASD and how do we know?**

# Pain Assessment in Autism

**73 ASD children/adolescents vs 115 controls**

- Behavioral, physiological (heart rate: HR), and plasma beta-endorphin (BE) pain responses**
- Matched for age, sex, pubertal status**
- 3 settings: home, school, during a venipuncture**

**Response to venipuncture:**

- Higher plasma BE and HR in ASD vs controls (both  $p < 0.05$ )**
- Absent/low behavioral reactivity in ASD (41%) vs controls (9%) ( $p < 0.0001$ )**
- Correlation between serum BE and HR**

**Tordiman et al; PLoS One, 2009**

- **Dissonance between pain sensitivity and pain reactivity:**
  - **Increased plasma BE levels and heart rates in ASD vs controls despite less behavioral reactivity in ASD vs controls**
- **Setting impacts pain reactivity:**
  - **22% ASD normally reactive to venipuncture vs**
  - **78% ASD normally reactive to burning (home)**

- **ASD individuals may experience more ongoing stress than controls**
  - **Higher plasma BE than in controls: plasma (not central) BE as a stress response hormone**

# Pain Assessment in ASD

**Venipuncture pain reactions videotaped in 21 ASD & 22 control children**

- Parent observer reports of pain**
- Coded facial activity (objective behavioral measure of pain)**

Nader et al; Clin J Pain. 2004

# Pain Assessment in ASD

## Results:

- facial pain reactivity: ASD > controls
- Parent ratings of behavior: no sig difference between ASD & control parents
- No concordance betw parental reports & observed pain responses
  - Concordance: controls > ASD

# Pain Sensitivity

- **ASD children have more tactile, taste/smell sensory abnormalities and sensory filtering problems than do other children with developmental delays** (Wiggins, et al 2009)



# Pain Sensitivity

- **Sig difference between ASD and controls in presence/frequency of sensory symptoms**
  - **greatest difference in under-responsivity, followed by over-responsivity and sensation seeking** (Ben-Sasson et al, 2009)
- **Sensory abnormalities very common in young children with autism** (Klintwall et al, 2011)

## Pain Assessment Summary

- **ASD individuals do not have decreased sensitivity to pain**
- **Less support for opioid theories of autism**
  - **absence of real endogenous analgesia**
  - **absence of clear benefits of opiate antagonist therapies**
  - **inconsistent results of studies measuring central opioid levels in autism**

# Pain Assessment Summary

- **Enhanced biological and physiological stress responses are dissociated from observable emotional and behavioral reactions**

# Contributors to Pain in ASD: Sleep Problems

- **Large population based longitudinal study in Norway 6-9 and 11-13 year olds: ASD vs controls**
- **Sleep problems 10 times higher in ASD than in controls**

## Contributors to Pain in ASD: Sleep Problems

- **Sleep problems increased over time: at wave 2 of cohort 37.5% in ASD vs 8.6% in controls**
- **Sleep problems more persistent over time: remission rate 8.3% in ASD vs 52.4% in controls**
- **Conclusion: Sleep is a sig problem in ASD and insufficient restorative sleep impacts pain sensitivity and tolerance**

# Contributors to Pain in ASD: GI Problems

- **Parent-rated questionnaire in 137 children with ASD and 112 healthy controls** (Smith et al, 2009)
  - **Bowel problems: 35% ASD vs 4% controls**
- **Questionnaire based survey of 412 children with autism vs cohort of 43 age-matched siblings** (Horvath et al, 2002)
  - **84% ASD vs 31% controls had  $\geq 1$  bowel symptoms**

## Contributors to Pain in ASD: GI Problems

- **Medical records evaluated in 137 children in an autism clinic for history of bowel symptoms**
  - **24% with  $\geq 1$  chronic bowel symptom**
  - **Most common symptoms: diarrhea and constipation**
  - **2% with pain (via medical record)**

**Molloy et al, 2003**

## Contributors to Pain in ASD: GI Problems

- **Lactase deficiency not associated with intestinal inflammation or injury is common in autistic children and may contribute to abdominal pain**
  - **65% of 199 ASD children with lactase deficiency**
  - **Lactase activity declined with age ( $p < 0.02$ )**
  - **Boys had 1.7 fold lower lactase activity than girls**
  - **On biopsies only 6% had intestinal inflammation**



## **Contributors to Pain in ASD: GI Problems**

- **Gastrointestinal problems with motility, sensitivity, and/or allergies are common in individuals with autism**
- **Visceral hyperalgesia likely common in this population**
- **Pain with eating or defecation can lead to food aversion or chronic constipation**
- **Abdominal pain can lead to ongoing altered behaviors**

## Contributors to Pain in ASD: GI Problems

- **Recommendations of a pediatric autism consensus conference**
- **Considering pain and look for medical reasons for pain in individuals with autism who have changes in behavior (“setting event”)**
- **When medical evaluations, especially of the gastrointestinal tract, are negative for defined pathology, visceral hyperalgesia should be considered as a cause of abdominal pain**

# Oxytocin (OT), Pain & Autism

**Converging evidence that OT increases trust, empathy, eye contact, face memory, and generosity** (Domes et al., 2007b; Guastella et al., 2008; Kosfeld et al., 2005; Savaskan et al., 2008; Zak et al., 2005; Zak et al., 2007)

**OT reduces the amygdala activation following threatening stimuli** (Kirsch et al., 2005)

**OT effect on amygdala activation more evident in response to social threats (faces)** (Kirsch et al., 2005)

# Oxytocin (OT), Pain & Autism

**Marked reduction in OT in children with autism relative to age matched controls**

(Modahl et al., 1998)

**Relative to placebo, OT administered intranasally to high functioning autistic patients improved eye contact, social memory, and use of social information**

(Andari et al.; Guastella et al., 2009a; Hollander et al., 2007; Hollander et al., 2003)

**Females have greater OT than males**

**Autism males 3:1 females**

## Oxytocin, Social Support and Pain

- **Social support has been shown to be a buffer for stress and for pain**
- **If individuals with autism have lower levels of oxytocin and difficulties in utilizing social support, one key pain buffer is unavailable to people with autism**
- **Autism may be a risk factor for development of chronic pain in part because of inability to access a key environmental component of pain reduction, social support**

# Pain and Autism

- **There is a disconnect between biological and behavioral pain responses**
  - **Apparent hyposensitivity reflects behavioral dissonance with pain experience**

# Pain and Autism

- **Parents report high levels of GI concerns (e.g. constipation, diarrhea) but lower concerns about pain (in questionnaires)**
- **Parents, caretakers, medical personnel may not be the best reporters of pain in individuals with autism**

# Pain and Autism

- **Difference in pain expression compared to non-autistic individuals is related to difficulties with:**
  - **verbal communication**
  - **body representation**
  - **problems representing sensations and emotions**
  - **problems establishing cause-effect relationships**



# Pain and Autism

- **High prevalence of GI symptoms in autistic individuals**
- **Hi prevalence of lactase deficiency but low prevalence of GI inflammation**

# Pain and Autism

- **Suggestion of high prevalence of visceral hyperalgesia and irritable bowel syndrome in autism**
  - **Neuroenteric dysregulation leading to hypersensitivity of intestinal tract (functional abdominal pain) or pain with constipation, diarrhea and/or other GI symptoms (IBS)**

## Pain and Autism

- **Self-injurious behaviors may be behavioral manifestations of experienced pain (attempts at reducing pain by creating other pain: as in descending noxious inhibitory control or DNIC)**
- **Oxytocin may play role in pain networks in individuals with autism**

# Pain and Autism

- **Pain may be a problem in autism also because of:**
  - **High prevalence of visceral hyperalgesia causing abdominal pain**
  - **Difficulty filtering sensory stimuli**

# Pain and Autism

- Perseveration on symptoms**
- Difficulties in self-soothing**
- Obstacles to seeking social support to help reduce discomfort**
- Increased anxiety and arousal that, in turn, increases pain**

# Pain and Autism

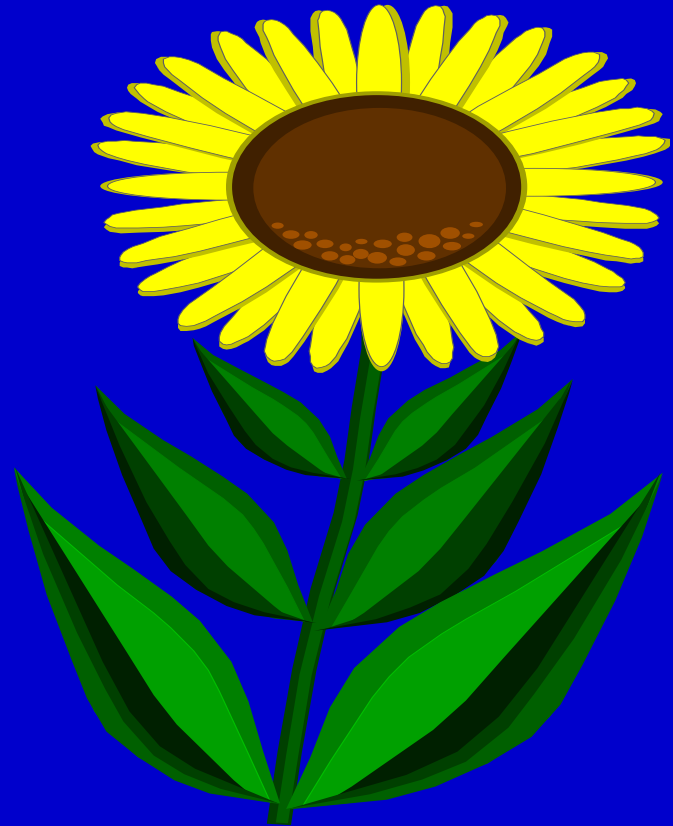
- **Need to develop better methods of assessing pain in autistic individuals and treatments aimed at potential mechanisms**

# Pain and Autism

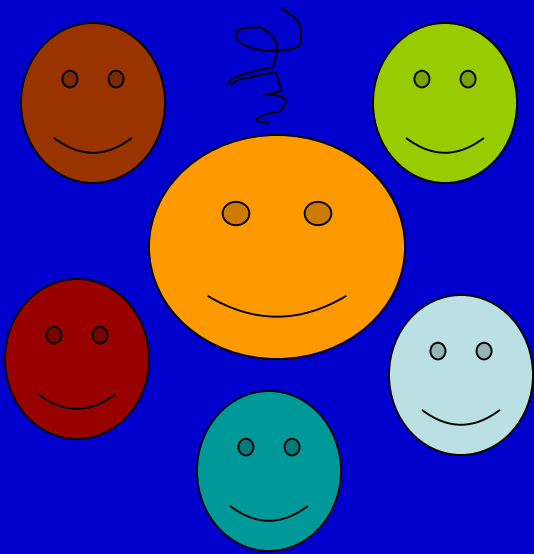
- **Need to target pharmacological therapies at pain and anxiety, as well as reducing perseveration, which leads to more anxiety and more focus on the pain**
- **Pharmacotherapy of pain is complicated by high incidence of side effects and need to start in very low doses**

# Complementary Medicine

- Hypnotherapy
- Acupuncture
- Iyengar Yoga
- Biofeedback
- Massage Therapy
- Relaxation Training
- Art Therapy
- Music, Dance,
- Drama, Writing
- Meditation







**Family support is key to good pain management in individuals with autism**