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)

Tordiman et al; PLoS One, 2009
• ASD individuals may experience more ongoing stress than controls

  - Higher plasma BE than in controls: plasma (not central) BE as a stress response hormone

Tordiman et al; *PLoS One*, 2009
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 between parental reports & observed pain responses

• Concordance: controls > ASD

Nader et al; Clin J Pain. 2004
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

Silvertsen et al, 2011
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

Silvertsen et al, 2011
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 ≥ 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

Kushak et al, 2010
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

Buie et al, Pediatrics, 2010
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
- High 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.