BEST OF PEDIATRIC PAIN RESEARCH: CHRONIC PAIN PAPERS

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Disclosures

- I have no conflicts of interest to disclose.

Two Studies in Pediatric Chronic Pain

- Simons, Pielech, Erpelding, Linnman, Moulton, Sava, Lebel, Serrano, Sethna, Becerra, & Borsook (2014). The responsive amygdala: Treatment-induced alterations in functional connectivity in pediatric complex regional pain syndrome. *Pain*, 155: 1727-1742.
- Horst, Shelby, Anderson, Acra, Polk, Saville, Garber, & Walker (2014). Predicting persistence of functional abdominal pain from childhood into young adulthood. *Clinical Gastroenterology and Hepatology*, 12: 2026-2032.

Simons, et al. (2014)

- Pain involves several neural networks tied to sensation, motor activity, cognition, and emotion
  - Growing interest in the cognitive and emotional aspects of pain with the amygdala as key region of interest (emotional arousal circuitry)
- Alterations in amygdala connectivity identified in adult pain samples
- Very limited application of fMRI research in pediatrics
  - Examine objective evidence of efficacy of treatments by changes produced in the brain

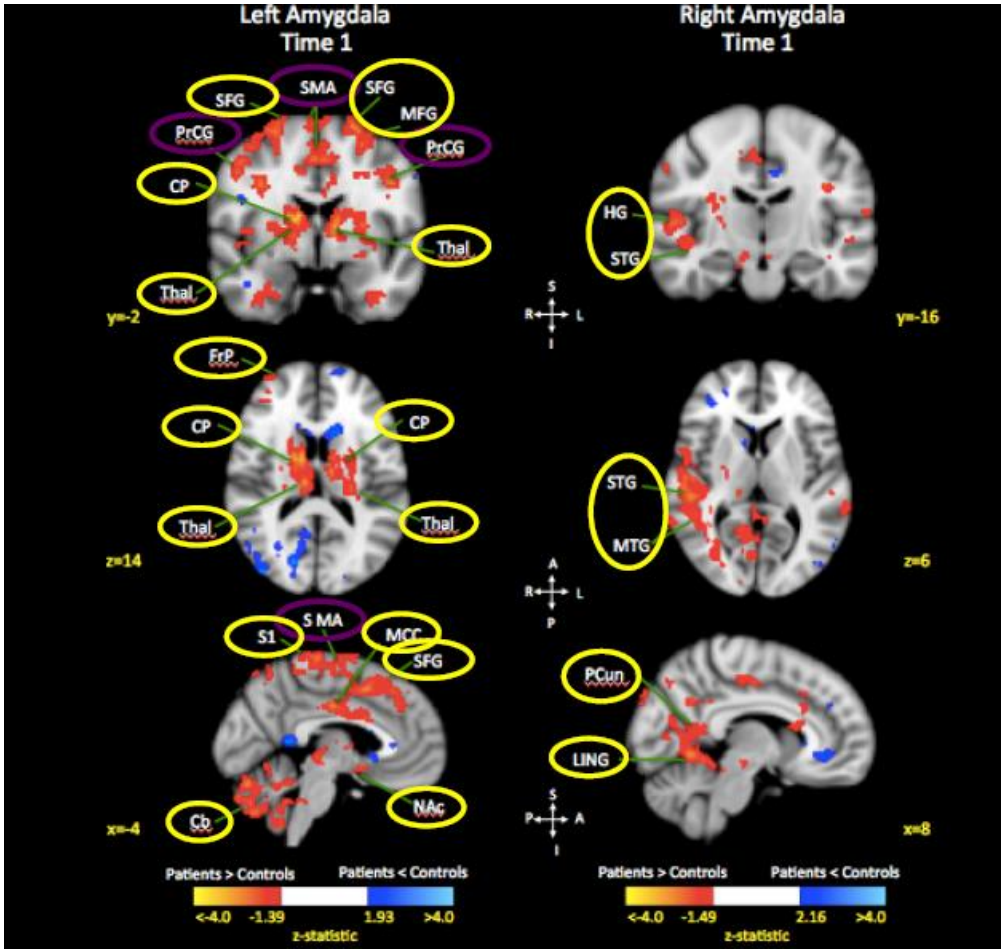
Study Aims

- Characterize and compare functional connectivity of the amygdala with the rest of the brain in pediatric complex regional pain syndrome (CRPS) and healthy control subjects
  - N = 12 in each group (ages 10-18 yrs)
- Examine changes that occur with chronification of pain and treatment after intensive pain rehabilitation (3 weeks)
  - Time 1 to Time 2 treatment effects

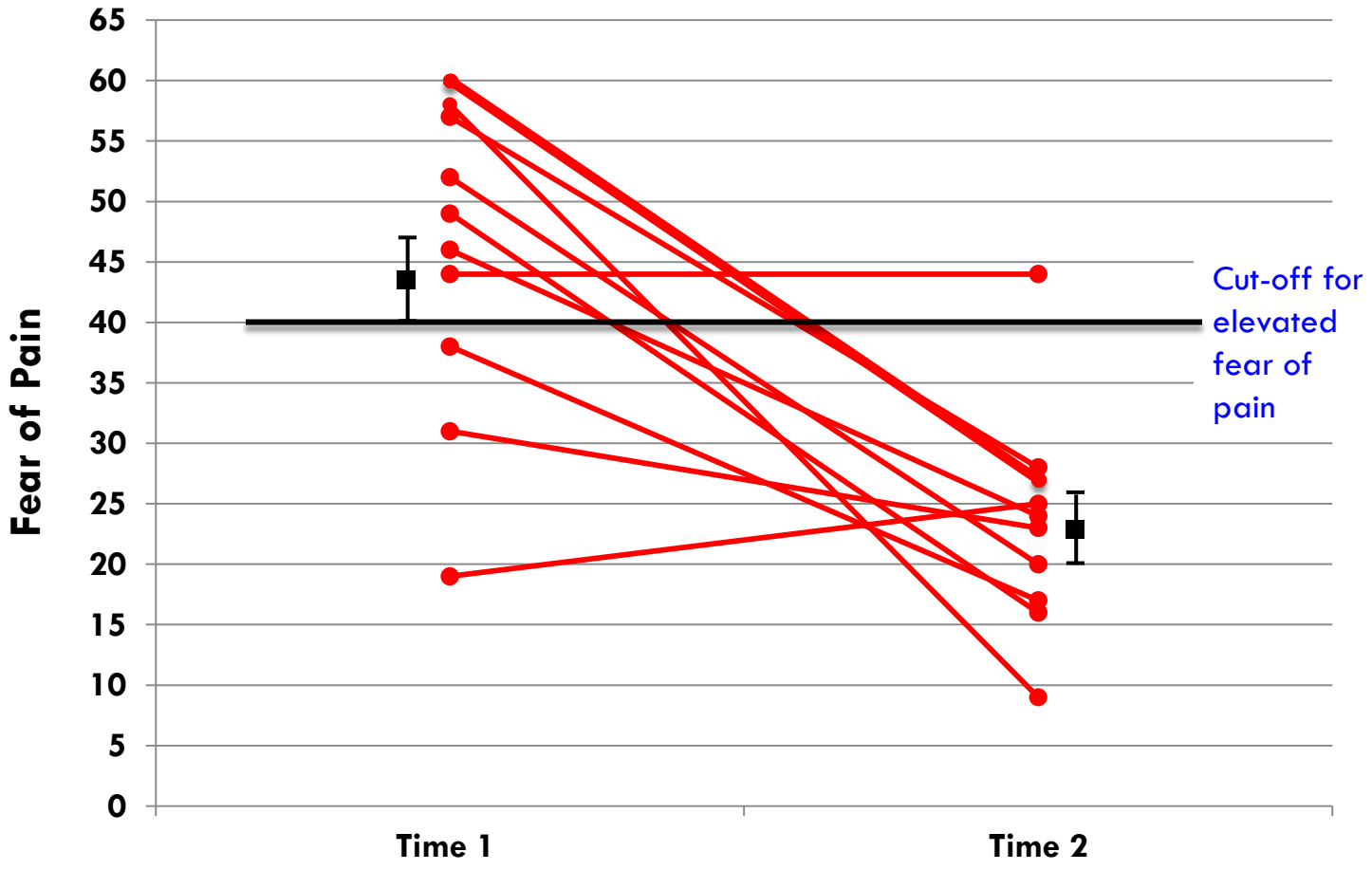
Summary of Findings

- **Disease state:** Enhanced amygdala connectivity in pediatric CRPS patients.
- **Treatment effect:** Weakened connectivity between left amygdala and several brain regions.
- **Fear circuitry:** Correlated with pain-related fear ratings.
- **Correlated activity:** Changes in intrinsic brain functional connectivity were linked to pain-related fear symptom improvement.

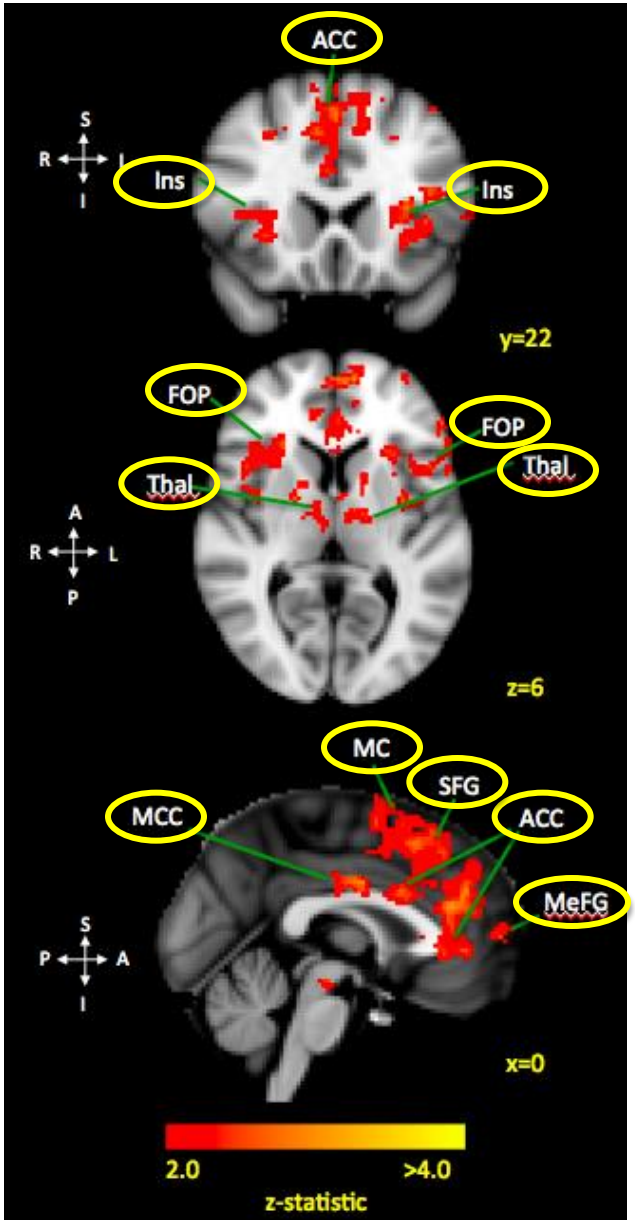
Disease state: Patients show heightened connectivity compared to controls.



Treatment response: Pain-related fear decreases



Treatment response and decreases in pain-related fear correlate.



Horst, et al. (2014)

- Few available longitudinal studies demonstrate that chronic abdominal pain may persist from childhood to adulthood
- Little is known about characteristics of symptom presentation in childhood that may predict long-term adolescent and adult outcomes
  - Many patients experience high rates of extraintestinal somatic complaints and psychological symptoms (comorbidities)

Study Aims and Methods

- Do extraintestinal somatic symptoms and depressive symptoms prospectively predict functional gastrointestinal disorders (FGID) in adulthood?
  - N = 392 participants, ages 8 – 16 years at initial evaluation $\longrightarrow$ evaluated 4 to 15 years later (average 9 years later)
  - Assessed depression on the CDI
  - Assessed somatic (GI and non-GI) symptoms on the CSI
  - Presence of Rome III FGID symptom criteria at follow-up evaluation

Main Findings

- 41% met Rome III symptom criteria for FGID at follow-up
- Regression model to test baseline predictors of FGIDs at follow-up
- Each additional extraintestinal symptom reported at baseline increased likelihood of FGID at follow-up

Table 3. Results of Multivariable Cubic Spline Logistic Regression Model Evaluating the Association of Each Childhood Factor With the Presence of FGID in Adolescence and Young Adulthood

Childhood factor	χ^2	*P* value
Depressive symptoms	12.38	.006
Extraintestinal somatic symptoms	6.00	.049
GI symptoms	7.87	.049
Abdominal pain severity	0.69	.88
Age at initial evaluation	2.08	.55
Sex	2.57	.11
Follow-up period, *y*	4.05	.26

Secondary Findings

- CDI score > 12 (cutoff for risk of depression) was nearly 3 x as likely to meet FGID symptom criteria at follow-up compared with a child with a CDI score < 4 (25% percentile)
- Nonlinear relationship was significant
- At CDI scores higher than 13 probability of FGID remained fairly constant

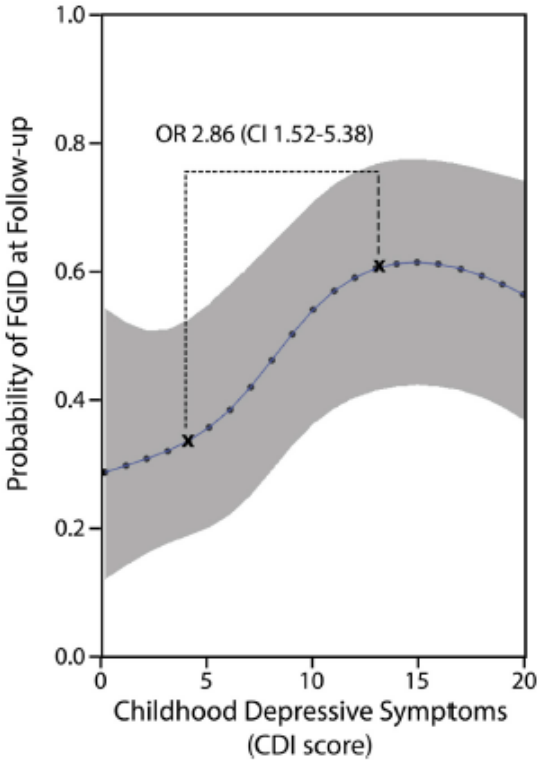


Figure 2. The probability of FGID at follow-up evaluation in adolescence or young adulthood based on baseline scores on the CDI, fixing all other variables to constant values (using the average value of each variable, or, if a categoric variable, using the model-based reference group). The odds ratio (OR) between the 25% and 75% interquartile values of the CDI scores is shown. CI, confidence interval.

Conclusions

- Several areas of emerging research in pediatric chronic pain
- Applications of laboratory and fMRI methods
- Focus on co-occurring pain and mental health disorders
- Longitudinal study of risk
- Implications for assessment and treatment of pediatric chronic pain