CHANGES IN BRAIN MICROSTRUCTURE WITH THE CHRONIFICATION OF PAIN IN YOUTH AT FAMILIAL RISK FOR ANXIETY AND DEPRESSION

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Introduction

- Chronic pain (> 3 months) in childhood is highly prevalent [1]
- Internalizing symtoms (ie., anxiety, depression) are highly comorbid with chronic pain and may be explained by alterations to shared neural connectivity underlying these conditions [2]
- Chronic pain in youth at familial risk for internalizing symptoms may associated with increased white matter connectivity between brain regions involved in both pain and emotional processing

Objective

- Examine whether differences in white matter microstructure, mainly FA and ADC are associated with the occurrence of pain in youth at familial risk for internalizing symptoms.

Methods

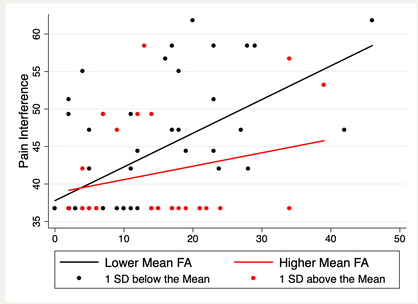
- Youth aged 11-18 years at risk for anxiety and depression underwent a 3T MRI scan
- Diffusion tensor images were obtained, and mean fractional anisotropy (FA) values and apparent diffusion coefficient (ADC), measures of white matter microstructure, were extracted from the corpus callosum (genu, body, and splenium), cingulum, inferior fronto-occipital, superior longitudinal and uncinate fasciculi
- Youth reported pain frequency, and were categorized into chronic pain (N = 30), acute pain (N = 22), or no pain groups (N = 60)
- Pain interference,[3] and internalizing[4] were reported using validated measures
- Univariate analyses were conducted to compare characteristics across the no pain, acute pain and chronic pain groups
- Regression analyses were applied to examine relationships between brain microstructure and pain interference, controlling for anxiety symptoms
- Examined in PROCESS whether brain microstructure together with internalizing symptoms was associated with pain interference

Results

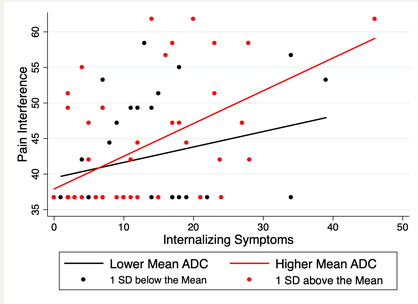
Cohort Characteristics

	Total (n=112)	No pain (n=60)	Acute Pain (n=22)	Chronic Pain (N=30)	*P* value
Age	13.7 (1.6)	13.8 (1.6)	13.4 (1.6)	13.7 (1.4)	0.71
Gender					
Female	69	38	12	19	0.75
Male	43	22	10	11	
Parent Education					
Some High School/ HS	9	6	0	3	
Diploma	27	15	5	7	0.26
Some college/University	17	9	0	8	
Trade	39	20	10	9	
Undergraduate Degree	19	10	6	3	
Some post-graduate work/post grad	1		1		
Other					
Pain Interference	43.2 (8.2)	38.8 (4.8)	44.9(7.8)	50.6 (8.4)	<0.001
Internalizing Symptoms	13.5(9.7)	11.4 (9.0)	15.4 (9.6)	16.3 (10.5)	0.05
Mean FA	0.46 (0.05)	0.45 (0.05)	0.45 (0.04)	0.48 (0.05)	0.13
Mean ADC	2.93 (0.07)	2.94 (0.07)	2.95 (0.05)	2.91 (0.06)	0.05

Linear Regressions



Mean FA 0.41 at 16th Percentile, p<0.001 (**black** line)
Mean FA 0.46 at 50th Percentile, p< 0.001
Mean FA 0.51 at 84th Percentile, p = 0.04 (**red** line)



Mean ADC 2.87 at 16th Percentile, p=0.02 (**black** line)
Mean ADC 2.93 at 50th Percentile, p < 0.001
Mean ADC 3.00 at 84th Percentile, p < 0.001 (**red** line)

	Pain Interference (N=112)		
Factors	ß	Standard Error	P-value
Age	-0.006	0.37	0.93
Gender	0.07	1.20	0.36
Parent Education	-0.15	0.36	0.37
Internalizing Symptoms	0.35	0.06	<0.001
Pain Type	0.54	0.67	<0.001
Mean FA	-0.17	11.49	0.02
	$R^2 = 0.51$		

Lower FA (ß =-0.17, *P*=0.02) and higher internalizing symptoms (ß=0.35, *P* <0.001) are associated with greater pain interference (R^2= 0.51)

	Pain Interference (N=112)		
Factors	ß	Standard Error	P-value
Age	-0.013	0.37	0.85
Gender	0.06	1.21	0.42
Parent Education	-0.14	0.36	0.04
Internalizing Symptoms	0.34	0.06	<0.001
Pain Type	0.55	0.68	<0.001
Mean ADC	0.16	8.59	0.03
	$R^2 = 0.51$		

Higher ADC (ß =0.16, *P*=0.03) and higher internalizing symptoms (ß=0.34, *P* <0.001) are associated with greater pain interference (R^2 = 0.51)

Conclusions

- Lower FA and higher ADC alongside greater internalizing symptoms were associated with greater pain interference in youth
- White matter connectivity was most impacted in youth with acute pain
- Higher anxiety in combination with an acute pain event may enhance risk for developing chronic pain
  - Significant rewiring following an acute pain event may lead to the chronification of pain
- These findings support the notion that youth at familial risk for internalizing symptoms should be asked about pain
- Introducing pain coping strategies for youth with higher internalizing symptoms may be of benefit and could prevent the development and maintenance of chronic pain

References

[1] Reitsma et al. Chronic Dis Inj Can. 2011; 31(4):157-164.
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[4] Ebesutani et al. J Clin Child & Adolesc Psychol 2011; 40(2):338-346.

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