Brain changes with chronic pain and exposure to adverse childhood experiences in youth

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Background

- Chronic pain is highly comorbid with internalizing mental health conditions, including post-traumatic stress disorder (PTSD). It had been demonstrated that youth with chronic pain have clinically significant elevations in post-traumatic stress symptoms (32%) as compared to their pain-free peers (8%).[1]
- This may be due to changes in shared brain networks, which are activated in response to both trauma and pain, including the corticolimbic circuitry (e.g., cingulum and uncinate fasciculus).[2,3] MRI studies shows changes of the microstructural integrity of the white matter, and altered functional brain networks in people who suffers form PTSD.[4,5]
- Emotion regulation is the ability of people to modulate their emotional state and expression. It had been demonstrated that the connections of the corticolimbic circuitry affect the emotion regulation.[6] Chronic pain is also associated with altered emotion regulation, specifically changes in cognitive reappraisal and expressive suppression, which might affect the pain indirectly, but through psychological factors such as depressive mood or anxiety.[7,8]
- Maladaptive emotional regulation strategies can increase the risk of youth who experienced adverse childhood events (ACEs) to suffer from PTSD and post-traumatic stress symptoms (PTSS).[9]
- Numerous white matter regions of interest were proposed in the literature as targets for changes along with anxiety and depression related disorders.
- However, it is unclear whether white matter changes due to traumatic exposure are associated with elevated risk for other chronic pain conditions in youth.

Objectives

- Our goal was to examine whether chronic pain, greater ACEs and PTSS were associated with changes at the white matter connectivity, and whether adaptive emotion regulation was neuroprotective.

Methods

- Youth aged 14-18 years were recruited via community advertisements. The participants underwent an MRI at the Alberta Children's Hospital twice, three months apart.
- During the MRI session, diffusion tensor imaging (DTI) was acquired. From the DTI, fractional anisotopy (FA) values of 11 white matter tracts were obtained. FA is an index of white matter connectivity, which increases with greater white matter maturation.
- Following the MRI, youth were asked to answer online questionnaires regarding basic demographics, medical history, pain, PTSS, emotional regulation and total number of ACEs.
- Generalized Estimating Equations were used to examine the relationships between chronic pain, ACEs, PTSS, emotion regulation and mean FA for each tract, accounting for age and gender.

Results

Cohort Characteristics

	Visit 1 (N=40)	Visit 2 (N=30)	*P* Value
Age	15.9 (1.5)	16.3 (1.5)	0.32
Female, n (%)	23 (57.5%)	15 (50.0)	0.26
White, n (%)	24 (60.0)	18 (60.0)	1.00
Chronic pain, n (%)	9 (22.5)	4 (13.3)	0.07
Pain interference	58.4 (11.3)	57.6 (11.5)	0.76
ACE's	2.5 (2.2)	2.6 (2.4)	0.84
PTSS	17.9 (16.7)	15.1 (17.4)	0.31
PTSS interference	0.26 (0.3)	0.22 (0.3)	0.32
Suppression	12.1 (3.5)	12.4 (4.0)	0.38
Reappraisal	19.1 (4.1)	18.8 (4.4)	0.37

Mean (standard deviation) displayed unless otherwise indicated.

- At baseline, 23% (9/40) of youth reported having chronic pain.
- Chronic pain and greater expressive suppression were associated with higher mean FA of the Corpus Callosum (Genu, Body and Splenium [Fig. 1*A-C*]) bilateral Cingulum (Fig. 1*D*), and the bilateral Uncinate ($p < 0.05$) (Fig. 1*F*).
- Higher ACEs score were associated with higher mean FA of the left Uncinate (Fig. 1*F*), and the right Superior Longitudinal Fasciculus (Fig. 1*G*) ($p < 0.05$).
- Greater PTSS interference was associated with lower mean FA of the right Cingulum (Fig. 1*D*), and the left Uncinate (Fig. 1*F*) ($p < 0.05$) .
- Greater cognitive reappraisal was associated with lower mean FA of the Inferior Fronto-Occipital Fasciculus (Figure 1*E*), left Uncinate (Fig. 1*F)* and the Superior Longitudinal Fasciculus (Fig. 1*G*) ($p < 0.05$).

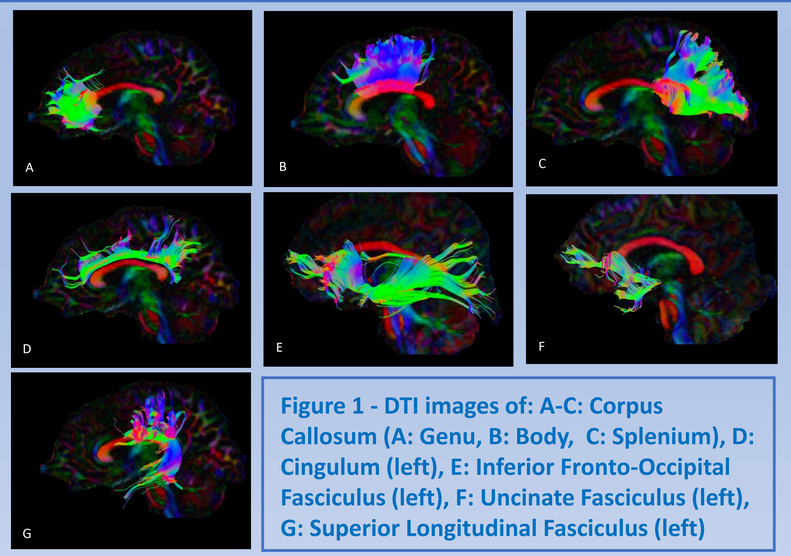

Figure 1 - DTI images of: A-C: Corpus Callosum (A: Genu, B: Body, C: Splenium), D: Cingulum (left), E: Inferior Fronto-Occipital Fasciculus (left), F: Uncinate Fasciculus (left), G: Superior Longitudinal Fasciculus (left)

Conclusions

- Chronic pain, suppression of emotion and greater exposure to ACEs were associated with higher mean FA, while higher cognitive reappraisal was associated with lower mean FA.
- These findings may imply a protective effect of emotion regulation within white matter tracts that have connections to the limbic system and connections to language pathways.
- Greater PTSS interference was associated with lower mean FA of the left Uncinate and the right Cingulum. Among individuals with greater PTSS, mean FA values within these regions were lower as compared to the mean FA values in individuals with higher cognitive reappraisal. Thus, the lower mean FA associated with PTSS appears to be potentially damaging versus protective.
- It is important to study FA within the context of both aversive and protective factors to better interpret changes in connectivity in the developing brain.
- Pain and mental health measures were stable within the youth in this sample between the two research visits. However, greater pain and trauma symptoms were associated with significant structural brain changes. These brain changes may contribute to the maintenance of these conditions over time.
- These findings contribute further to the growing knowledge regarding the mutual connections between the life-events, emotional regulation, chronic pain and their effects on the white matter connectivity.
- By improving emotion regulation in youth, we may be able to prevent the development and maintenance of pain and mental health problems via age-appropriate development of the white matter.

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