

Functional brain changes associated with improvements in outcomes following intensive pain rehabilitation in youth

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INTRODUCTION

Severe Pediatric Chronic Pain:

- Highly prevalent and significantly impacts daily functioning
- Leads to persistent pain and mental health struggles in adulthood, placing undue strain on healthcare systems (1)
- Involves greater engagement of emotional processing brain regions and less engagement of sensory regions compared to acute pain (2)
- Research in pediatric patients with complex regional pain syndrome indicates worse symptoms correlate with lower levels of emotional centre activation (3)

The Intensive Pain Rehabilitation Program (IPRP):

- Youths undergo 3 weeks of multimodal day-treatments
- It is not well understood how these types of programs influence brain changes in youth

Hypothesis 1:
IPRP will be associated with an increase in brain activity in response to emotional stimuli

Hypothesis 2:
Changes to brain activity will be associated with improvements in pain interference

METHODS

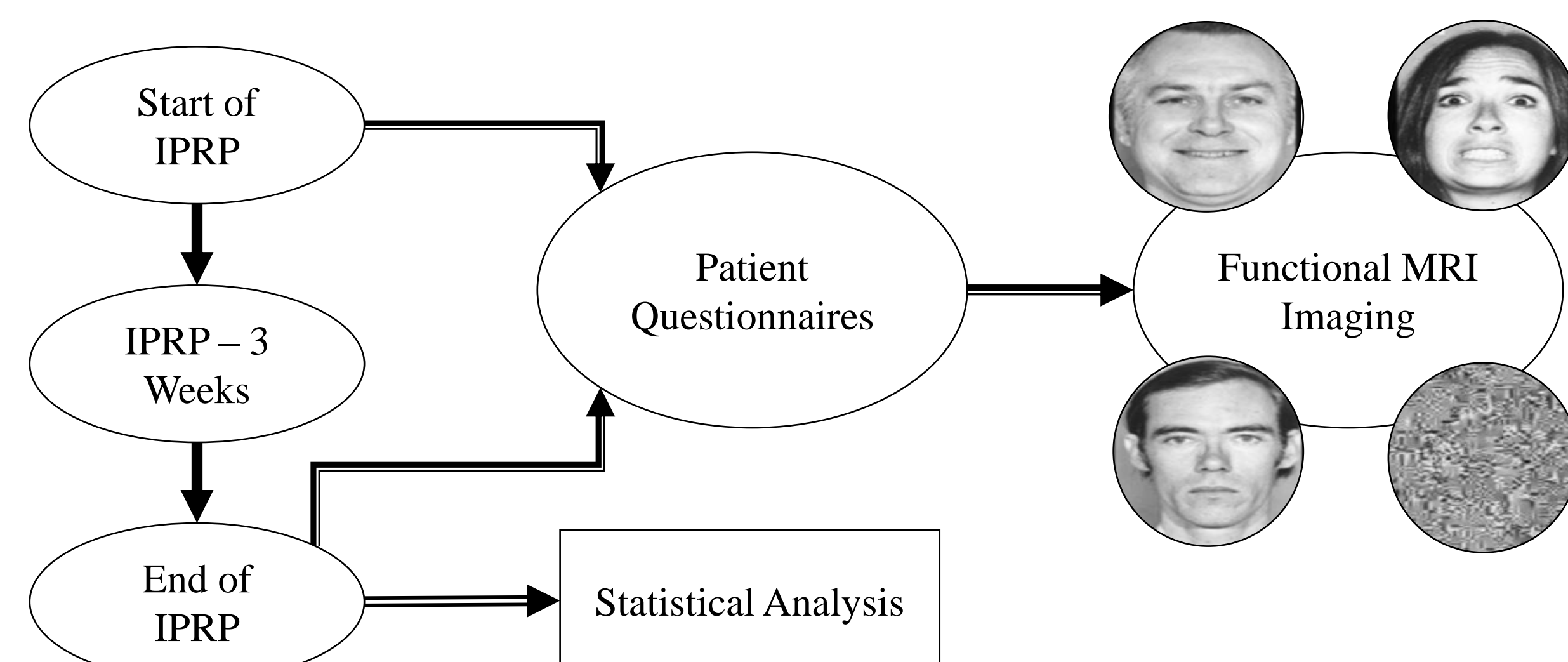


FIGURE 1

Project Workflow. Patients completed a set of questionnaires and underwent fMRI imaging for response to emotional stimuli both pre- and post-IPRP. During scanning, patients were presented with emotional stimuli - faces expressing emotions such as happiness and fear, as well as neutral and scrambled images. Questionnaires covered pain type, intensity, and interference.

Statistical Analysis

- Paired t-tests performed on fMRI data to compare mean differences in brain responses to emotional versus neutral stimuli, pre- and post-IPRP
- Brain clusters demonstrating significantly different levels of activation following FWE correction were then extracted and linear mixed models were applied to examine changes in activity between pre- and post-IPRP MRI scan in relation to pain interference, accounting for patient age

RESULTS

TABLE 1. Cohort Characteristics

Characteristics	n = 20
Age, M (SD)	16.2 (1.3)
Female, n (%)	17 (85)
Baseline pain intensity, M (SD)	5.5 (2.0)

Primary Pain Complaint

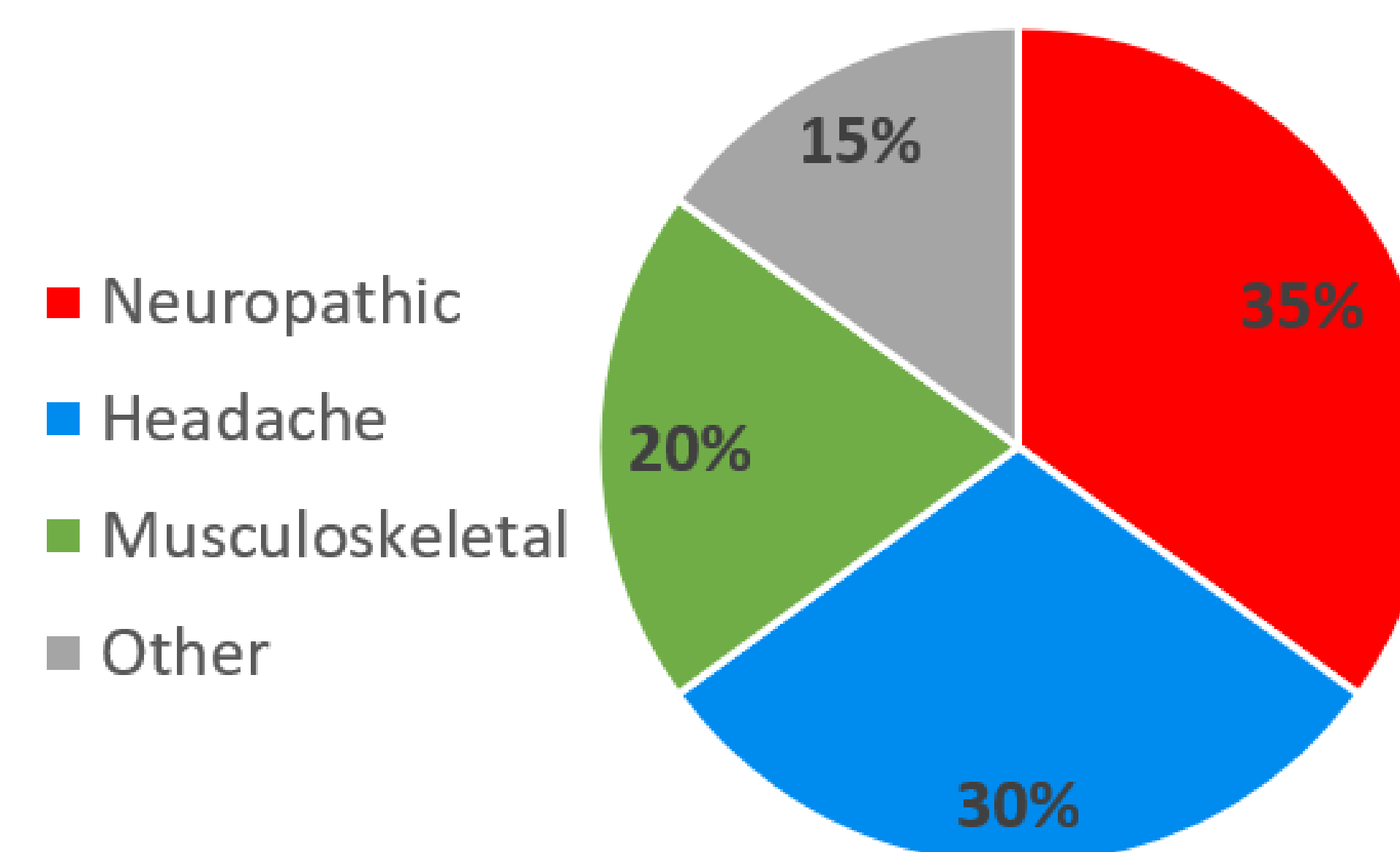


FIGURE 2

Proportion of primary pain complaint in participants in this study

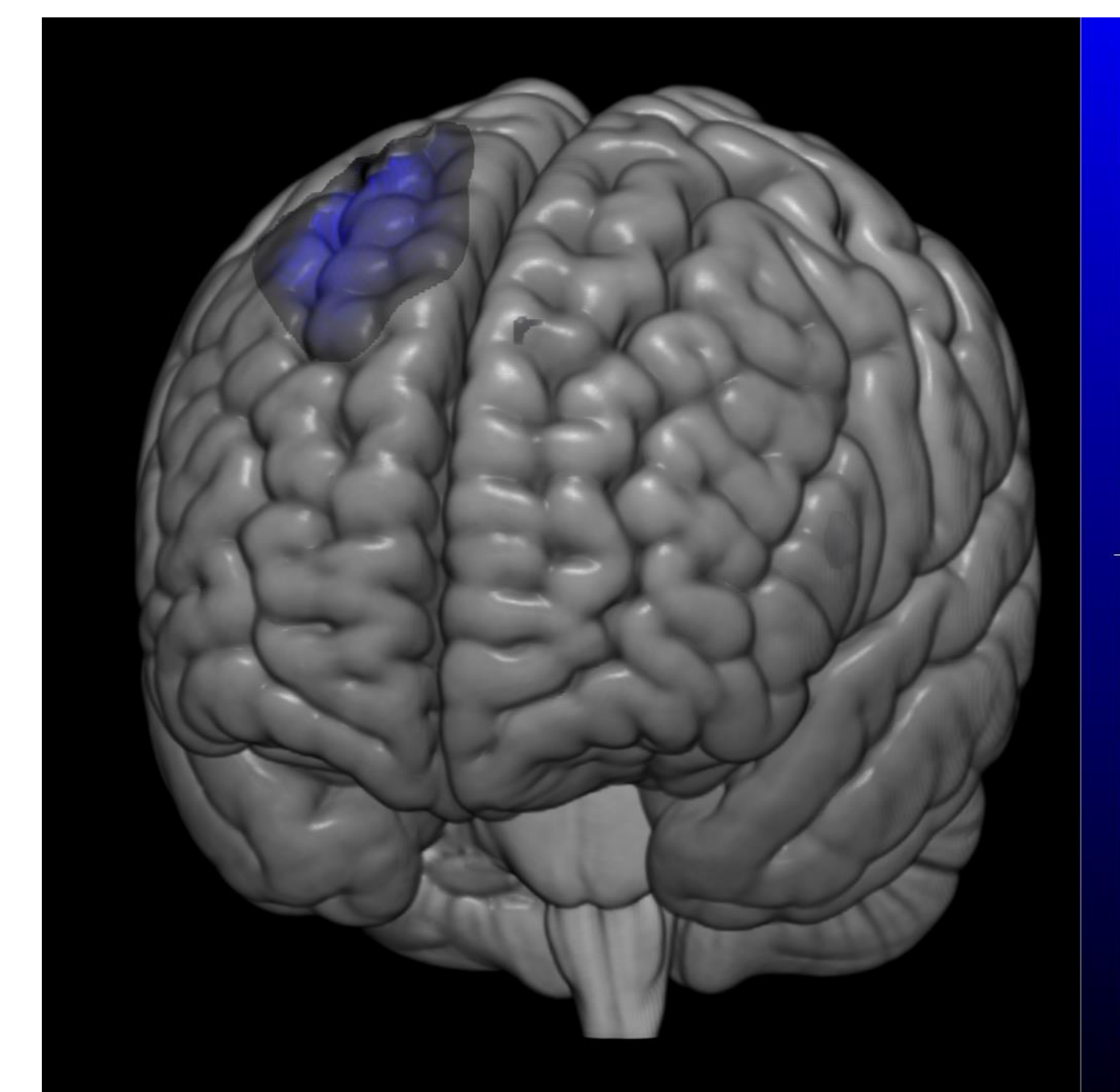


FIGURE 3

Decreases in Dorsolateral Prefrontal Cortex (DLPFC) activity from pre- to post-IPRP

TABLE 2. Change in DLPFC activation and pain interference (PI) pre- and post- IPRP

	Variables	Mean Difference	n	Std. Deviation	df	t	Significance (2-tailed)
Pair 1	'DLPFC 1' - 'DLPFC 2'	0.410	20	0.433	19	4.229	<0.001
Pair 2	'PI 1' - 'PI 2'	4.763	16	8.601	15	2.215	0.043

TABLE 3. Estimates of fixed effects on pain interference

Parameter	Estimate	df	t	Lower 95% CI	Upper 95% CI	P-Value
DLPFC	6.393	24.921	2.374	0.846	11.941	0.026
Age	1.491	17.997	1.111	-1.329	4.310	0.281

DISCUSSION & NEXT STEPS

Key results:

- IPRP was associated with significant **decreases** in the DLPFC activity in response to emotional versus neutral stimuli from pre- to post-IPRP
- IPRP was also associated with decreases in pain interference from pre- to post-IPRP
- Change in DLPFC activity was significantly associated with improvements in pain interference
- The DLPFC is pivotal to pain modulation, and cognitive and emotion regulation

Limitations:

- Small sample size, and therefore underpowered to detect whether decreases in DLPFC activity underlie decreases in other outcome metrics pre- to post-IPRP

Future Directions:

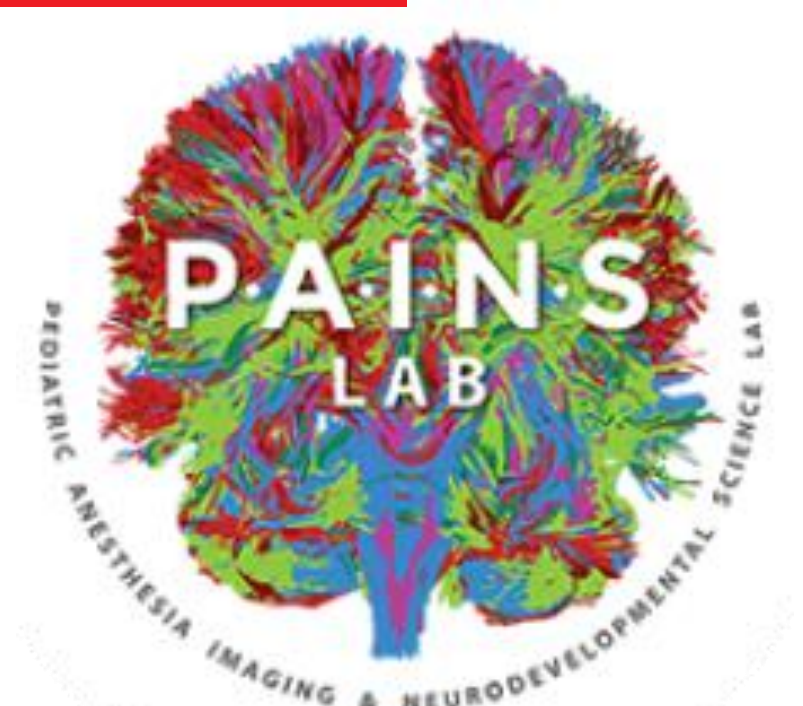
- The DLPFC is a common therapeutic target for brain stimulation.
- Currently, exploring the extent that repetitive transcranial magnetic stimulation of the DLPFC is able to enhance improvements associated with IPRP in youth with severe chronic pain

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