

Identifying the Impact of Centralized Pain on Pain Outcomes After Interventional Pain Procedures

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Background

Spine pain is the most common reason patients visit their doctor. Between 12-15% of the U.S. population seeks spine pain care each year with associated costs exceeding \$200 billion.

The term "centralized pain" has been used to describe any CNS dysfunction or pathology that may be contributing to the development or maintenance of chronic pain. The pain experienced by individuals with centralized pain is typically multifocal, rated as more severe, and characterized by neuropathic pain descriptors. Another hallmark of the centralized pain phenotype is the frequent presence of hyperalgesia and/or reduced or absent endogenous analgesia. Data from quantitative sensory testing (QST) studies suggest a wide, bell-shaped distribution in pain sensitivity across the general population. Most, but not all, individuals with centralized pain fall on the right side of this curve and have QST findings consistent with notable hypersensitivity (hyperalgesia and allodynia). There is growing appreciation of the importance of centralized pain in chronic pain states and the impact it has on potential poor analgesic outcomes after interventional procedures. Peripherally-directed pain interventions are postulated to be less effective for individuals with centralized pain without addressing the underlying CNS amplification.

Materials and Methods

OVERALL STUDY DESIGN

Prospective, observational study in patients who underwent an interventional pain procedure (epidural steroid injection or radiofrequency ablation in the spine). Baseline patient phenotyping was performed and assessed using numerical pain score, physical function, depression, anxiety, and fibromyalgia-ness validated measures

MEASURES

- Comprehensive Baseline Phenotyping
 - Demographics
 - Fibromyalgia-ness (FMness) - 2011 FM Survey Criteria
 - Clinical Pain – Brief Pain Inventory (BPI)
 - Neuropathic Pain Descriptors – PainDETECT
 - Psychiatric History/Status – PROMIS Depression & Anxiety
 - Functional Status – PROMIS physical functioning & PROMIS Pain Interference

STATISTICAL METHODS

Analgesic outcomes (AOC):
AOC-success: 50% reduction in pain severity scores from baseline to 3 months (a response more commensurate with the invasiveness of the intervention)
AOC-failure: < 50% reduction (difference between worst pain felt in the past week at baseline vs. at 3-month follow up)

Widespreadedness of pain:
Positive Test: three or greater areas of pain (out of 7 areas)

Table 1. Participant Survey Schedule

Domain	Instrument	Baseline	2 W F/U	1 M F/U	3 M F/U
Pre-Screen	Pre-Screen Form	X			
Consent	Informed Consent				
Eligibility	Eligibility form	X			
Enrollment	Enrollment	X			
Stop Study	Stop Study Form				
Withdrawal	Consent withdrawal				
Demographics	Demographics	X			
Diagnostics	2011 FM Survey Criteria (FM Score)	X	X	X	X
Pain	Brief Pain Inventory (BPI)	X	X	X	X
	PainDetect	X	X	X	X
Allied Symptoms	PROMIS Phys Function 4	X	X	X	X
	PROMIS Pain Interference 8	X	X	X	X
	PROMIS Depression 4	X			X
	PROMIS Anxiety 4	X			X
	Coping Strategies Questionnaire (Catastrophizing)	X			X
	Patient Global Impression of Change				X

Table 2. ESI Baseline Characteristics

Variable	Responder	n	Median	IQR	P-Value
FM Score	Non-Responder	48	10	5.25	0.00269
	Responder	13	5	5	
	Total	61	9	7	
BPI Worst	Non-Responder	49	7	2	2.93E-09
	Responder	20	3	3	
	Total	69	7	4	
BPI Average	Non-Responder	49	6	2	5.23E-09
	Responder	20	1.5	3	
	Total	69	5	3	
Pain Detect Score	Non-Responder	49	14	8	0.000178
	Responder	20	7	5.75	
	Total	69	12	10	
PROMIS Physical Function	Non-Responder	49	35.3	6.6	0.000133
	Responder	20	42.3	16.85	
	Total	69	37.2	7.3	
PROMIS Pain Interference	Non-Responder	49	64	6.3	0.000304
	Responder	20	57.1	14.5	
	Total	69	62.5	8.4	
PROMIS Depression	Non-Responder	49	52	21.2	0.0138
	Responder	20	41	14.425	
	Total	69	51.2	18.2	
PROMIS Anxiety	Non-Responder	49	49	19.4	0.0161
	Responder	20	40.3	10.35	
	Total	69	47.9	16.6	

Table 3. RFA Baseline Characteristics

Variable	Responder	n	Median	IQR	P-Value
FM Score	Non-Responder	17	14	8	0.0997
	Responder	3	4	5.5	
	Total	20	13	8.75	
BPI Worst	Non-Responder	17	8	1	0.00683
	Responder	4	3	2.75	
	Total	21	7	2	
BPI Average	Non-Responder	17	6	2	0.0701
	Responder	4	3	2.75	
	Total	21	5	3	
Pain Detect Score	Non-Responder	17	21	13	0.117
	Responder	4	9.5	8	
	Total	21	16	14	
PROMIS Physical Function	Non-Responder	17	34.9	4.7	0.00612
	Responder	4	49.2	15.7	
	Total	21	37	8	
PROMIS Pain Interference	Non-Responder	17	66.9	5.1	0.00617
	Responder	4	57	12.125	
	Total	21	65.7	6.5	
PROMIS Depression	Non-Responder	17	60.5	7.8	0.206
	Responder	4	44.95	11.675	
	Total	21	60.5	14.8	
PROMIS Anxiety	Non-Responder	17	59.5	9.5	0.367
	Responder	4	49.15	19.525	
	Total	21	58.7	11.8	

Results

- 18.7% of all participants were deemed to be responders with a 50% or greater pain severity score improvement over the trial period
- ESI non-responders had statistically significant greater fibromyalgia scores, brief pain inventory averages, pain detect scores, pain interference scores, depression and anxiety
- RFA non-responders had p-values approaching significance, but only had significantly greater values in 3 categories: brief pain inventory, physical function score, and pain interference
- Another analysis that defined a responder to interventional pain procedures as 30% or greater improvement in pain had similar data trends to when responders were categorized as >50% improvement in pain
- In a logistic regression analysis, a participant who had evidence of widespreadedness of pain was 43% less likely to have 50% improvement 3 months after an intervention compared to participants without widespread pain

Conclusions

- The study identifies that patients who respond positively to interventional pain procedures such as ESI and RFA are different at baseline compared to those who don't respond
- Those who did not respond had increased levels of widespread pain, fibromyalgianess, anxiety, depression, and neuropathic pain with decreased physical functioning and pain interference
- The results of this study should not lead practitioners to not perform peripherally directed pain interventions in patients with evidence of widespread pain and a more centralized pain phenotype, however, additional interventions aimed at nociplastic pain (centrally acting medications, physical activity and rehabilitation, and behavioral interventions) may be recommended in addition to interventional procedures
- This multimodal approach can address the ongoing central sensitization that will not be addressed through a peripherally directed intervention

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