Changes in pain catastrophizing predict changes in pain and vice versa in patients with neuropathic pain: A cross-lagged panel analysis study

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Introduction

- Catastrophizing is recognized as a key psychosocial factor associated with pain-related negative outcomes in individuals with chronic pain, accounting for 7 to 31% of variance in pain intensity [1-3]. Longitudinal studies are needed to better understand the temporal relationship between these constructs.
- Neuropathic pain (NeP) is one of the most difficult pain syndromes to treat pharmacologically [4, 5]. Consequently, there is a growing interest in understanding the influence of psychological factors such as catastrophizing on NeP outcomes.
- Even though it would be ideal if all patients had access to structured multidisciplinary pain treatment programs, most pain clinics have long waitlists and are often unable to offer non-pharmacological interventions that specifically address catastrophizing. Studies are therefore needed to determine if greater treatment resources should to be allocated to reduce catastrophizing in patients with NeP. A cross-lagged panel analysis approach in a large sample of longitudinal data can be a way of understanding the role and importance of catastrophizing in the treatment process.
- A small amount of previous research [3] has used cross-lagged panel analyses in patients with mixed pain problems and healthy subjects. The obtained results support the view that changes in catastrophizing predicted subsequent changes in pain intensity and interference, but not vice versa, in both multidisciplinary pain treatment programs and laboratory-induced pain.

Study Objectives

To determine wether:

- changes in pain catastrophizing that occur early in treatment predict subsequent changes in pain intensity and interference later in treatment.
- early changes in pain intensity and interference predict subsequent changes in catastrophizing in patients with NeP.

Hypothesis: Given theoretical consideration as well as previous research having examined these issues, we hypothesized that early changes in catastrophizing during treatment would predict later changes in pain intensity and interference, while the reverse relationship would not be found.

Methodology

Participants and study design

- As part of a larger prospective trial, 538 patients with NeP were recruited from six multidisciplinary pain clinics across Canada.
- The study sample consisted of patients with NeP who had completed self-administered measures of catastrophizing (Pain Catastrophizing Scale), average pain intensity (0 to 10 NRS) and interference (Brief Pain Inventory, short form) when first seen in the clinic and at 3-and 6-months treatment follow-ups (FU).

Main eligibility criteria

- NeP diagnosis confirmed by the clinic physician
- NeP is the primary diagnosis for ≥ 3 months
- Aged 18 years or older
- Anticipated life expectancy ≥ 2 years
- Able to complete a questionnaire in English or French
- Able to provide informed consent

Data analyses

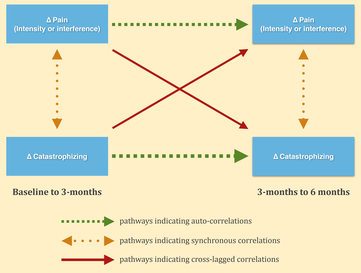
- A series of zero-order Pearson correlations were performed to examine the associations between catastrophizing, pain intensity and interference at baseline, 3-month, and 6-month FU.
- An ANOVA was used to determine whether all variables significantly improved across baseline to 3-month, 3-month to 6-month, and baseline to 6-month FU changes scores.
- Another series of zero-order Pearson correlations were performed using the residualized change scores to test the associations between baseline to 3-month and 3-month to 6month changes between catastrophizing and pain intensity and interference.
- Four linear regression analyses were performed, using residualized change scores, to test unique lagged associations between the variables of interest while controlling for extraneous sources of variance (auto and synchronous correlations).

Cross-Lagged Panel Analysis

The cross-lagged panel analysis approach provides a method to assess temporal associations between catastrophizing and pain while controlling for two extraneous sources of variance:

autocorrelation: correlation between the same variable at different time points and,

synchronous correlation: correlation between different variables that are measured at the identical time point



Results

As shown in Table 1, all variables were intercorrelated across time. In addition, baseline catastrophizing was moderately associated with all time-point measures of both pain intensity and interference.

Variable	1	2	3	4	5	6
1. Baseline pain	-	.62*	.60*	.52*	.41*	.39*
2. 3-month pain	.57*	-	.70*	.37*	.56*	.46*
3. 6-month pain	.51*	.67*	-	.40*	.48*	.54*
4. Baseline catastrophizing	.43*	.29*	.27*	-	.69*	.68*
5. 3-month catastrophizing	.39*	.47*	.39*	.69*	-	.71*
6. 6-month catastrophizing	.38*	.41*	.53*	.68*	.71*	-

Table 1: Zero-order correlations between pain intensity, pain interference and catastrophizing at baseline, 3-month and 6-month treatment follow-up. Pain Intensity; Pain Interference; * $p < 0.001$

As can be seen in Table 2, we observed significant reductions in pain intensity, pain interference, and catastrophizing from baseline to 3-months. We also found a significant reduction in both pain intensity and catastrophizing (albeit lesser, relative to the first three months) at 3- to 6-months. The 3- to 6-month decrease in pain interference was not statistically significant. Consistent with these findings, the results also showed a statistically significant overall improvement in outcomes after receiving treatment at the pain clinics from baseline to 6-month across all of the three study variables.

	Baseline to 3-months			3-months to 6-months			Baseline to 6-months		
	Mean	SD	p-value	Mean	SD	p-value	Mean	SD	p-value
Pain Intensity	6.11	1.91	< 0.001*	5.45	2.17	0.006*	5.21	2.28	< 0.001*
Pain Interference	6.02	2.43	< 0.001*	5.20	2.64	0.122	5.05	2.75	< 0.001*
Catastrophizing	24.84	12.45	< 0.001*	22.04	12.75	0.002*	20.67	13.24	< 0.001*

Table 2: Baseline, 3-month, and 6-month treatment follow-up change scores for pain and catastrophizing. * $p < 0.01$

The correlations between, pain intensity or pain interference and catastrophizing residualized change scores are presented in Table 3.

Variable	1	2	3	4
1. Δ baseline to 3-month pain	-	0.18**	0.48**	0.01
2. Δ 3-month to 6-month pain	-0.12*	-	-0.03	0.52**
3. Δ baseline to 3-month catastrophizing	0.36**	0.04	-	-0.26**
4. Δ 3-month to 6-month catastrophizing	0.03	0.39**	-0.26**	-

Table 3: Zero-order correlations between baseline to 3-month and 3-month to 6-month treatment follow-up residualized change scores. Pain Intensity; Pain Interference; * $p < 0.01$; ** $p < 0.001$

Table 4 depicts the linear regression analyses, testing whether changes in baseline to 3-month catastrophizing accounted for significant variance in 3-month to 6-month pain intensity or pain interference above and beyond extraneous sources of variances, and vice versa.

Cross-lagged 1 – A: 3-month to 6-month change in pain intensity was significantly associated with both baseline to 3-month change in pain intensity (autocorrelation) and 3-month to 6-month change in catastrophizing (synchronous correlation), accounting for 17% of extraneous variance. More importantly, a unique cross-lagged correlation was found between baseline to 3-month change in catastrophizing and 3-month to 6-month change pain intensity, accounting for an additional 5% of the variance when controlling for all extraneous variance (Full model: $R^2 = 0.22$, $p = < 0.001$).

Cross-lagged 1 – B: Baseline to 3-month catastrophizing (autocorrelation) and 3-month to 6-month pain intensity (synchronous correlation) were both significantly associated with 3-month to 6-month catastrophizing, accounting for 23% of extraneous variance. More notably, a significant unique cross-lagged association was observed between baseline to 3-month pain intensity predicting 3- to 6-month change in catastrophizing, accounting for additional increment of 4% (Full model: $R^2 = 0.27$) of the variance.

Cross-lagged 2 – A: Similarly to pain intensity, baseline to 3-month pain interference (autocorrelation) and 3-month to 6-month catastrophizing (synchronous correlation) were both significantly associated with the 3- to 6-month change in pain interference, accounting for 33% of the explainable variance. A unique cross-lagged association was also observed between baseline to 3-month catastrophizing and a 3- to 6-month change in pain interference, accounting for an additional 6% of the total variance (Full model: $R^2 = 0.39$, $p < 0.001$).

Cross-lagged 2 – B: Comparable results were also obtained for baseline to 3-month catastrophizing (autocorrelation) and 3- to 6-month pain interference (synchronous correlation), accounting for 33% of extraneous variance. A cross-lagged relationship was observed between baseline to 3-month pain interference and the 3- to 6-month change in catastrophizing, incrementing the variance by an extra 7% (full model: $R^2 = 0.40$, $p < 0.001$) while controlling for extraneous variance.

In summary, all four unique cross-lagged correlations significantly accounted for 4% to 7% of the total variance of regression models, representing a small to moderate effect size (*r*s range between 0.20 to 0.26).

Cross-lagged 1

A. Dependent variable: Δ 3-month to 6-month pain intensity	B (SE)	t-ratio	p-value
Δ 3-month to 6-month catastrophizing	0.46 (0.04)	10.84	< 0.001*
Δ baseline to 3-month pain intensity	-0.22 (0.04)	-4.99	< 0.001*
Δ baseline to 3-months catastrophizing	0.24 (0.05)	5.25	< 0.001*
B. Dependent variable: Δ 3-month to 6-month catastrophizing	**B (SE)**	**t-ratio**	**p-value**
Δ 3-month to 6-month pain intensity	0.43 (0.04)	10.84	< 0.001*
Δ baseline to 3-month catastrophizing	-0.36 (0.04)	-8.37	< 0.001*
Δ baseline to 3-months pain intensity	0.21 (0.04)	4.96	< 0.001*

Cross-lagged 2

A. Dependent variable: Δ 3-month to 6-month pain interference	B (SE)	t-ratio	p-value
Δ 3-month to 6-month catastrophizing	0.59 (0.04)	15.33	< 0.001*
Δ baseline to 3-month pain interference	-0.32 (0.04)	-7.53	< 0.001*
Δ baseline to 3-month catastrophizing	0.28 (0.04)	6.37	< 0.001*
B. Dependent variable: Δ 3-month to 6-month catastrophizing	**B (SE)**	**t-ratio**	**p-value**
Δ 3-month to 6-month pain interference	0.59 (0.04)	15.33	< 0.001*
Δ baseline to 3-month catastrophizing	-0.39 (0.04)	-9.52	< 0.001*
Δ baseline to 3-month pain interference	0.30 (0.04)	7.22	< 0.001*

Table 4: Cross-lagged panel design results between change in catastrophizing and pain. * $p < 0.001$

Conclusions

- The present findings indicate that early treatment decreases in catastrophizing precede subsequent improvements in pain intensity and interference, and early treatment improvements in both pain intensity and interference precede decreases in catastrophizing.
- The results are consistent with theoretical models hypothesizing a causal impact of catastrophizing on pain intensity and interference, and suggest mutual causation among these factors.
- Importantly, the present results also support catastrophizing as a primary treatment target that could influence other important outcomes, and also suggest the possibility that treatments that target and reduce pain intensity or pain interference could potentially influence catastrophizing. Therefore, there may be multiple paths to obtain positive outcomes.
- Research aiming to investigate other cognitive process factors and comparing their ability to predict pain-related outcomes are needed to identify additional treatment targets.

Main study limitations:

- Because treatment is tailored to each patient's unique NeP syndrome, the design does not allow us to determine the treatment components (if any) that led to the improvements in study factors.
- We were not able to control for potential confounding factors.
- The sample consisted entirely of patients with NeP, therefore the results may not generalize to other type of chronic pain problems.
- These results may also not reflect the reality of individuals being treated in primary, secondary, interdisciplinary pain care, or in pain treatment facilities outside of Canada.

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