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The Stressful Characteristics of Pain that Drive you N.U.T.S.: A qualitative exploration of a stress model to understand the chronic pain experience

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ABSTRACT

Despite decades of research on the identification of specific characteristics of situations that trigger a physiological stress response (Novelty, Unpredictability, Threat to ego, Sense of low control; N.U.T.S.), no integrative research has examined the validity of this framework applied to pain experiences. This study aimed to (1) explore stressful characteristics of pain among individuals living with chronic pain and (2) examine whether the N.U.T.S. framework comprehensively captures the stressful nature of pain.

Subjects were 41 adult participants living with chronic pain.

Six focus groups were conducted in French using a semi-structured interview guide. Participants first discussed how pain is stressful. Then they were introduced to the N.U.T.S. framework and commented on the extent to which it captured their experience. Interview verbatim was analyzed with a reflexive thematic analysis. Analyses were conducted in French; quotes and themes were translated into English by a professional translator.

The Pain-N.U.T.S. framework adequately captured participants' experience. Multiple aspects of pain (pain intensity fluctuations, pain flare duration, pain quality and location, functional limitations, diagnosis and treatment) were associated with one or more stress-inducing characteristics. In addition, a second layer of meaning emerged in the context of chronic pain that provide contextual information regarding when, how, why pain became more, or less stressful.

The N.U.T.S. characteristics seem to offer a comprehensive framework to understand how pain and its context of chronicity can be a source of stress. This project provides preliminary support for the Pain- N.U.T.S. framework that allows to formally integrate pain and stress research.

INTRODUCTION

The experience of stress can have paradoxical effects on pain (hyperalgesia/hypoalgesia) (1-3). When the brain detects a threat, it sets off a sophisticated multi-system reaction, including activation of the hypothalamus-pituitary-adrenal (HPA) axis (4, 5) that culminates in the production of glucocorticoids (4, 5). Stress has been connected to multiple chronic pain conditions (e.g., back pain, migraine); in some ways chronic pain could be understood as a self-intensifying stressor contributing to *allostatic load*, a measure of chronic stress (6). Given the impact of stress on pain, it is crucial to prevent the cascade of physiological responses to stress as to lessen the stress-pain bidirectional amplification.

There is an overwhelming amount of literature on appraisal of pain as a stressful experience and its association with important constructs such as pain catastrophizing and coping.(7) Surprisingly, little attention has been spent on understanding the characteristics of pain itself that might trigger a physiological stress response and influence pain appraisal. In the general stress literature, decades of research have identified four specific characteristics (8, 9) of situations that systematically activates the HPA axis: Novelty, Unpredictability, Threat to the ego (socio-evaluative threat), and Sense of low control. Each time the brain perceives the presence of one or more of these characteristics, it will trigger a physiological stress response (10). Novelty refers to situations that are encountered for the first time and trigger the physiological stress response regardless of whether they are predictable or unpredictable (e.g., moving to a new house could be perceived as novel and predictable). Unpredictability refers to situations for which the outcome is uncertain (e.g., participating in a competition) or the timing of occurrence is unknown (e.g., pain flare up). Threat to the ego refers to one's integrity or sense of self being under perceived threat whereas sense of low control refers to situations over which individuals perceive (whether or not this is

actually the case is irrelevant here) having no control. These four characteristics were grouped together under the acronym N.U.T.S. by Lupien (10) to facilitate integration of knowledge of situational characteristics that trigger a physiological stress response and knowledge translation efforts.

Some studies have examined these components individually in the context of pain. *Novelty*: Evidence demonstrates that the reduced novelty induced by repeating predictable pain stimulation at low frequency may produce site-specific reductions in pain sensitivity (11, 12). Novel pain sensations are also associated with greater pain interference (13, 14). *Unpredictability*: Unpredictable spontaneous pain fluctuations are associated with increased pain intensity and variability, and pain avoidance in experimental settings (13, 15-18). Among clinical populations, less predictability of pain occurrences is associated with hyperalgesia (17, 19, 20). *Threat to ego*: In laboratory settings, threatening social contexts facilitate pain-related fear learning (21) or threat (22), pain intensity (23) and can influence salience of noxious stimuli and modulate pain experience (24). *Sense of control*: Experimental studies suggest that an enhanced sense of control over pain does not reduce pain intensity but rather lessens the affective dimension of pain (25-28). Clinically, perceived lack of control is associated with worse pain outcomes (29, 30).

To date there has been no systematic investigation of the N.U.T.S. framework among chronic pain patients. Qualitative inquiries (31) appear particularly suitable as an initial step to identify various dimensions in the pain experience that are perceived as stressful, leading to the development of more comprehensive ways of measuring and understanding this phenomenon (32).

This study aimed to (1) explore stressful characteristics of pain from the perspective of the lived experience of individuals suffering from chronic pain and (2) examine whether the N.U.T.S. model comprehensively captures the stressful nature of pain. This knowledge will contribute to support

an emerging integrative framework that links psychosocial and neurobiological models of pain and stress and propose a new avenue for interventions.

METHODS

2.1 Study design

This is a qualitative study involving six semi-structured focus group interviews with individuals living with chronic pain conducted in the research center of a downtown Montreal hospital (Canada) in May and June 2019. Team members have expertise in pain research and come from the fields of health (psychology, neuroscience, neuropsychology) and social (sociology) sciences. The study was approved by the research ethics board of the Centre hospitalier de l'Université de Montréal (18.368-YP). Guidelines for qualitative research (Consolidated Criteria for Reporting Qualitative Studies (COREQ)) were used to report this study (33).

2.2 Participants

A total of forty-one participants were recruited from the *Association Québécoise de la douleur chronique*, a patient association, through an email sent to their members. Another 12 participants were scheduled but did not show for the focus group or cancelled their participation. Interested participants provided their contact information through an online registration form and were then contacted by phone by a research assistant who assessed eligibility and enrolled them in one of the focus groups. Participants were eligible to participate if they were adults (18 years old or above), spoke fluent French, had been experiencing non-cancer related pain for 3 months or longer with a mean pain intensity over the past week $> 3/10$, lived in the province of Quebec and were able to attend an in-person group meeting. Exclusion criteria included presence of severe cognitive/physical impairments that made it impossible for them to complete questionnaires or engage in group discussions.

2.3 Procedure

Participants took part in one focus group that varied in size between 4 and 8 individuals. This is consistent with recent recommendations on optimal sizes for focus groups (34). Each group offered a mix of genders and age groups (see Table 1). Focus groups were favored over individual interviews as we wished to explore the co-construction and dynamic, evolving perspectives of participants as they pondered on their experience of chronic pain as a stressful phenomenon (34). Interviews were conducted using a semi-structured guide and divided into two parts and revised after the first focus group. In the first part, participants were asked to generally discuss the characteristics of their pain experience that they find stressful. In the second part, participants were introduced to the N.U.T.S. model and asked to comment more directly on how the different components of the model represented their experience of pain as being stressful. Focus groups were between 2 to 2.5 hours in duration. Informed consent and basic socio-demographic and pain characteristics were obtained from all participants before the beginning of the focus group using a self-reported questionnaire. The conversations were audio-recorded and transcribed verbatim. Each participant was assigned a pseudonym to use during the focus group to facilitate transcription of the interview and to protect participants' confidentiality. Participants received 50\$ as a compensation for their time and parking/transportation fees.

The focus groups were led by the first author (MGP), a female pain psychologist and researcher with several years' of experience in pain research, trained in quantitative and mixed methods. She was supported by ED, a female sociologist trained in qualitative research and a research assistant who took behavioral observations during the interviews. Participants were recruited until

theoretical saturation was reached. There was no a priori relationship between researchers and participants. Participants were told at the time of recruitment that the research team was interested in learning about their experience of pain and stress. They were aware that the research team was multidisciplinary and of the background of the researchers. No other information regarding the interviewers' characteristics were shared with participants.

2.4 Translation

The original focus groups were conducted in French. Following recommendations for qualitative analysis and publications of findings in another language than the original research,(35) we took the following steps to minimize meaning lost in the translations of quotes and themes: 1) conducting the analyses in the original language until the writing up of the manuscript, keeping fluid descriptions of concepts using various English formulations until almost the end of analysis and with discussions among team members, and the collaboration between a professional translator and one author (MGP) to translate quotes and main study themes into English.

2.5 Data analysis

A dominantly reflexive thematic analysis (36), using patterns of shared meaning but also domain summaries, was the favored method of analysis. We adopted a blended approach to data analysis whereby we cycled between inductive and deductive approaches.(37, 38) Concept-driven coding (deductive approach) was used initially since we knew a priori the themes that we were interested in analyzing (N.U.T.S.). However inductive coding was also used in order to identify dimensions of pain in which the N.U.T.S. characteristics could be identified as well as how the broader context of pain chronicity influenced the expression of these N.U.T.S. characteristics. More specifically,

we initially identified sources of stress shared by participants to understand their nature. We evaluated whether these characteristics were relevant to the existing N.U.T.S. framework or whether they were representing unidentified dimensions of stress. The inductive approach was particularly important to explore additional characteristics present in the data that did not fit with the N.U.T.S. framework and that could complement or inform us about the fit of this framework to capture the stress experience. (36) Contextualization of these characteristics within the broader lived experience of participants was explored inductively using patterns of shared meaning. We focused on stressful characteristics of pain specifically to answer the stated objective. General discussions of stress unrelated to the pain experience were not subject of analysis.

The analysis was led by the first author (MGP) who initially read all the transcripts several times to gain a detailed understanding of the participants' experiences. Transcripts were coded in NVivo12 (39) using domain summary to capture the elements that compose each of the N.U.T.S. characteristics as applied to pain. Two focus group transcripts were coded by another team member (LD or ED) who both have experience with qualitative data analysis. This led to the creation of the preliminary and evolving codebook.(40) Moving toward an interpretive level of analysis, transcripts were coded with emergent themes using in-vivo, process and open codes through line-by-line analysis and axial coding to explore relationships among existing themes.(41) The first author adopted an iterative approach whereby she navigated multiple times between the raw data and her interpretations and reflections of participants' experiences. Frequent meetings between these three team members (MGP, LD, ED) and regular memo writing (identification of variations in participants' narratives for each theme, testing hypotheses, exploring rival explanations) helped reduce risks of subjectivity bias and increase validity of data interpretation. (33, 42)

2.5 Characteristics of participants

A total of 41 participants took part in one of six focus groups. Sixty percent of participants (n=25) were female and participants were between the ages of 32 and 78 years old (median = 57 years old). There was a wide variation in pain duration (between 1 and 52 years living with pain). Pain was in multiple body sites for all but 5 participants. Table 1 shows the demographic and pain characteristics of participants overall and per focus groups.

RESULTS

As shown in the results below, The N.U.T.S. characteristics, applied to pain (referred to the Pain-N.U.T.S. framework) comprehensively captured the stressful nature of pain. Six specific themes related to the pain experience emerged as being favorable to the occurrence of one or more N.U.T.S. characteristics (see Fig. 1) and formed the core of the analyses presented here. However, in a second, more distal layer of meaning, participants discussed how these stressful characteristics are also experienced within a broader stressful context that emerges not directly from the noxious sensations, but rather from the chronicity of their pain condition (see Fig. 2). This second layer aims to provide context regarding the appraisal of stress and impact of the N.U.T.S. characteristics of pain in the context of pain chronicity.

We describe both interconnected layers below.

Level 1 of the Pain-N.U.T.S. framework: Stressful characteristics of the pain experience

During the focus groups with participants and in the analysis, no experience of pain-related stress was described that could not be categorized into one of the four N.U.T.S. characteristics of stress. The experience of N.U.T.S. characteristics were present in six different aspects directly related to the pain experience, namely pain intensity, pain location and quality, duration of pain episodes, functional limitations, management and treatment, and diagnosis (see Fig. 1).

Fluctuations in Pain Intensity

Variability of pain intensity was identified as stressful by most and in multiple contexts, in part because of the unpredictability associated with these fluctuations. Peaks of pain intensity that arrived without warnings were particularly threatening to participants.

- Ⓚ “I have peak moments of pain; there are some things that I know are going to end up causing a peak. At one point I find one: if I push too hard, if I walk too

much, you know. But there are times when it just happens, and I don't know why..." (Begonia, 32 y.o.; 5 years living with pain, focus group 6)

Those peaks of pain intensity also did not have the same impact on the individual's sense of self depending on their context of occurrence, for example whether the person was alone at home or in a social gathering.

Ⓣ "Well, there's the social aspect, too, because when I... because when I'm in pain, I bend over at the waist, I really... It puts me in a situation where everyone is wondering what's going on... 'Why? What can I do?'... You can't do anything it's just that it hurts!"
(Venus, 62 y.o., 37 years living with pain, focus group 1)

Many participants felt like they had little control over the experience of pain in general, and this was particularly true when they perceived being unable to influence pain flares.

Ⓢ "... I've never been someone who gets all that stressed out, but there's a pain that creates... because I expect that it's going to get worse, and I don't have any control over it. And I like to have some control over what's going on in my life. But I don't have any control over that." (Eagle, 77 y.o.; 13 years living with pain, focus group 2)

Many participants also reported having a sense of low control when they could accurately predict an increase in pain intensity.

Ⓢ "The link that I see, in relation to pain and stress, is that my stress is going to get worse when I've got a task to do, a task that is physical, a task that is, above all, important. A task that I've got to complete by a certain time. And I expect to have pain while I'm doing it. As we say, '*You expect pain,*' and that's like saying

‘Oh no, I know that that’s going to hurt,’ and that’s a problem.” (Spruce tree, 47 years old; 21 years living with pain, focus group 4)

Surprisingly, no participants described fluctuations of pain unpleasantness as being stressful.

Pain location and quality

Even though all participants had chronic pain and most had pain for over a decade, they reported variations in the location and quality of pain that heightened their threat perception. Sometimes, this stress was associated with the novelty of a pain location that was beyond their familiar, typical pain location.

Ⓝ “Well for me, it’s my lower back, the sacrum. Then at some point my pain starts climbing. When it starts going up, we say it’s because my lower half doesn’t work. The top half is working harder, but then you end up with new kinds of pain, and it’s as if you’re afraid that it just won’t stop anymore. How far is it going to go this time, or get worse?” (Topaz, 55 y.o., 12 years living with pain, focus group 3)

Other times this stress was associated with variations in terms of number of body sites affected by pain.

Ⓤ “One day you get up alright, and it can all be much more manageable. But if things aren’t going well, then it’s really hell. There are days when you’re fine, and then there are days when your body is attacking you. That’s what I call it. ‘I’m being attacked by my body.’ It’s the intensity of the pain, the number of places where you have pain... If one day it’s just your knees, then the next day

it's your arms, elbows, knees, hands... (laughing)..." (Earth, 44 y.o., 4 years living with pain, focus group 1)

For others, changes in the quality of their pain experience, or type of pain, brought on worries about the meaning attributed to these new symptoms and what they meant for the future.

Ⓝ “ Yes, that's right, because you wake up, you're like this and you think, 'Oh, that's not my pain.' That's what I tell myself. Let's say that today I'm not feeling well, but it's not my pain, not the one I know. It's some other pain that's there. What's going on, is it..." (Topaz, 55 y.o., 12 years living with pain, focus group 3)

When pain is located in specific parts of the body it could become particularly threatening for one's ego. This was reported in terms of threat to his social self but also in terms of his own sense of identity.

Ⓣ “In my case, I've been suffering for the last 5 years from interstitial cystitis, which is a chronic inflammation of the bladder at the urinary level, the genitals, the whole shebang. All the good things in life, you know what I mean? And they're working, but it hurts so much that they're not working for very long! So it's quite hard on one's ego, whether it's in relation to others or just with myself, when I'm at home alone.” (Earth, 44 y.o., 4 years living with pain, focus group 1)

Duration of pain flares

Above and beyond how long they have been suffering from pain, the presence of an acute exacerbation of their pain appeared to be a significant source of stress for most patients. This is in part attributed to the unpredictable length of such episode.

- Ⓚ “Then whether you want it or not, the stress kicks in, because you wonder, when is this going to end, all this pain (the group confirms it), you know, when is it going to end, the worst of the pain I’m going through right now!” (Oak, 34 y.o., 6 years living with pain, focus group 4)

In addition, participants’ sense of low control to manage pain during such exacerbation also added to the extent to which they found it stressful.

- Ⓢ “The way I see it, it’s like a wind that rises up from the desert but then arrives over a warm ocean, and this just encourages the heat welling from the ocean. Then the wind turns into a hurricane, faster than you would have liked. You see it coming, and you say to yourself (speaking softly), ‘What can I do? Should I take shelter?’ ” (Mars, 70 y.o., 2 years living with pain, focus group 1)

Functional limitations

Beyond the simple experience of pain sensations, how pain impacts their daily life and functioning was for all participants an important source of stress. Stressful characteristics associated with pain-related limitations were described as novel, unpredictable, threatening the ego and lacking perceived control.

Participants reported being challenged by new functional limitations directly associated with their pain condition.

- Ⓝ “And then it arrives, and with so much pain. It’s a new pain, so it’s really stressful because I’m at home, I can’t move, I can barely make it out of bed to

my chair in the living room. It's like... It's stressful, having something new..."

(Cricket, 56 y.o., 45 years living with pain, focus group 5)

Not being able to predict the outcome of a situation has almost been like a self-fulfilling prophecy for some participants whereby this apprehension increased stress which in turn increased pain.

Ⓚ "...And then it's going round and round in your head, and you say, 'OK, am I going to be alright tomorrow, am I going to be able to do the things I've planned?' This goes round and round in your head and then, whether you want to or not, well your brain sends signals to your body that exacerbate the pain."

(Poplar, 42 y.o., 11 years living with pain, focus group 4)

In addition, functional limitations seemed to have a direct impact on one's sense of self and this appeared to be particularly embedded in social contexts. In some instances it appeared impossible for participants to conform to what was socially expected of them, as for this mother.

Ⓣ "With the children, it's awful. My daughter is 9 years old. 'Mommy, you promised we'd do this! You told me we'd go!' 'Well yes, but Mommy isn't able to go, you see? Mommy's in a wheelchair today, you know?' I always get tears in my eyes, but it isn't easy for her, either. So I know that I'm becoming a burden for her (spoken in a trembling voice), but no matter what I may want, it's stressful for me, too. You're nervous, you're anxious." (Oak, 34 y.o., 6 years living with pain, focus group 4)

Finally, participants perceived having no control over functional limitations or little room for pushing past these limitations.

Ⓢ "You know, in life you decide to study, you work and everything, you make decisions. But then the pain arrives and you can't decide anything anymore,

except for the choices that are imposed on you.” (Willow tree, 61 y.o., 6 years living with pain, focus group 4)

Management and treatment

Participants described having to face the stress associated with the trial of a new therapeutic approach for their pain. The impact of novelty on pain-related stress lied in the uncertainty of both treatment success and possible associated side effects.

Ⓝ “When something comes along that you haven’t tried yet, there’s some fear. What’s it going to do for me, how much am I going to have to pay for it afterwards, is it going to work? There hasn’t been any treatment that’s worked so far. When you try something, you always have some doubts. Anything new, anything they bring you comes with a kind of stress. Anything that’s an unknown.” (Diamond, 57 y.o., 5 years living with pain, focus group 3)

Furthermore, the response to pain management and treatments was often unknown to participants and unpredictable. The same is true for participants’ interactions with the medical system; there was an inherent degree of uncertainty related to the clinicians’ responses to their pain.

Ⓞ “When you go to see a doctor, because you’re expecting something like you’d expect with any other medical concern... that when you go to see a doctor, there will be at least some potential solution. Not necessarily a solution, but a possibility to explore. But I think we can all agree that in this case, there’s nothing of the sort!” (Swallow, 52 y.o., 52 years living with pain, focus group 2)

Accessing medical treatments for pain was also received with incomprehension, helplessness or disbelief from the care providers, which was threatening for many participants.

- Ⓣ “Because being told by a doctor that you’re wrong, or that you’re making things up, and then there’s no question of throwing out the... I would just like to do some tests, to see. Is it going to make a difference, yes or no? Otherwise we go back to the old... dosage, and then that’s it. But at least we tried some things.” (Venus, 62 y.o., 37 years living with pain, focus group 1)

Additionally, participants described having little solutions to manage pain other than just very temporarily.

- Ⓢ “ No, I haven’t got any control over that. There’s nothing there, nothing we can do. I’ve gone through the list of all the specialists, all the drugs and all the clinicians.” (Eagle, 77 y.o., 13 years living with pain, focus group 2)

Interestingly, even for those who had access to some techniques or pharmacological approaches to manage pain, this was not perceived as having control over pain or their life.

- Ⓢ “Stress and pain, it is all intimately related. I’d say that, over the years I’ve learned that having control over my life is no longer possible for me, because it’s... what I do is manage my stress and manage my activities. It’s about managing, I’m always managing something!” (Owl, 50 y.o., 6 years living with pain, focus group 2)

The sense of low control was also discussed in the case of treatments that have been perceived as imposed on the individuals.

Ⓢ “What stresses me a lot, too, for me it’s all the different treatments that are imposed on me. We try one thing, and if it doesn't work, well I don't know what we’re going to do. OK, the transplant worked, but we’re going to try something else. We’re going to try such-and-such a drug. So now you have side effects, you know. It looks like you’re losing control of your body, too.”

(Oak, 34 y.o., 6 years living with pain, focus group 4)

Diagnosis

A new diagnosis could create doubts and apprehension about its meaning, persistence and evolution.

Ⓝ “Since September, they added... I don’t remember, another diagnosis, plus another diagnosis, in December, of fibromyalgia. So it’s like there are two other diagnoses in not even 6 months, in such a short period of time. So it’s like, OK, that’s a lot, and it’s causing me more stress.” (Mercury, 44 y.o., 9 years living with pain, focus group 1)

But participants also described that an existing diagnosis could also cast a shadow over new symptoms and lead to minimization of other possible underlying conditions.

Ⓝ “I try to control the pain by taking Dilaudid, but since I’m in a wheelchair, I’m putting a lot of strain on my shoulders. I’ve torn some tendons, but I never realized it because I was taking pain killers. I had some pain, but it was in my shoulder. I was using it, but I thought, ‘It isn’t serious, it’s not serious.’ But then at one point I had an ultrasound, and I had torn some

tendons. I have a bicep that has become a unicep.” (Venus, 62 y.o., 37 years living with pain, focus group 1)

Multiple investigations yielding inconclusive or contradicting results in the quest for a pain diagnosis were perceived as unpredictable.

Ⓚ “I’ve been going through a lot. For 11 years they’ve been trying to find what’s wrong with me. I’ve received diagnoses that were later ruled out... It seems like the system is always giving you hope that you’ll get back to a normal life, but in the end, ‘Poof!’ and it’s gone. Then they send you somewhere else, giving you more hope, and ‘Poof!’ it’s gone again” (Poplar, 42 y.o., 11 years living with pain, focus group 4)

Some diagnoses could carry their load of stigma and become a stressor that participants carried with them and threatened their ego.

Ⓚ “Today I understand that fibromyalgia is a catch-all term used by doctors when they don’t know what else to say. And the first thing you hear, and that you read, too, is ‘Oh yes, it’s the disease of the lazy.’ Oh boy...” (Swallow, 52 y.o., 52 years living with pain, focus group 2)

For all these six dimensions of pain-related stress, there were also important differences between participants, consistent with the subjective, personal nature of stress and pain. Indeed, the same situation did not trigger the same stress response across individuals. For example, while some participants found it stressful to be isolated without anyone who could give them a hand, others found the experience of pain in front of others very stressful.

“When I’m in intense pain, I’d like it if someone would help me, give me some guidance. That gives me some relief. I’m... I’m the opposite of him. I like it when someone helps me.” Crystal (59 y.o.; 2 years living with pain, focus group 3)

“.” Ruby (77 y. o.; 21 years living with pain, focus group 3)

Level 2 of the Pain-N.U.T.S. framework: Pain-related stress in the context of chronicity

This second level of analysis aims to complement the N.U.T.S. framework described in Level 1 by examining the different ways through which the chronicity of one’s pain condition can influence one’s appraisal and reactions to the stressful characteristics identified in Level 1.

Above and beyond the inherent stressful characteristics of pain, individuals described with great emphasis the role of pain chronicity in their perception of pain-related stress.

“I see it as... In fact, chronic pain should be considered a disease. But I also have pain that comes every day, every week, every month, or whatever.” (Hornet, 68 y.o., 28 years living with pain, focus group 5)

The context of chronicity went beyond the inherent stressful characteristics of pain described in level 1 in that they included the effects of time, sense of self in the context of living with a chronic illness, and contextual and systemic factors.

One’s and others’ reactions to pain as it persisted through time changed and support typically eroded. Participants described different aspects of pain progression that provided some insights to understand *WHEN* chronic pain was stressful. This dimension was inherently related to time, namely the impact of chronicity and persistence of pain and associated experiences over time. In addition, they also explained *WHY* pain became stressful, particularly in the context of amplifications of pain through incompatible needs and accompanying loss of identity. This dimension reflected primarily the impact pain had on their sense of self. They continued describing

HOW stress-related pain occurs, namely through the individual and systemic influences of pain perception, including meaning attribution, stigma and negative social encounters. This cumulating stress related to their pain experiences pushed many participants to develop strategies that could serve as a buffer to protect themselves from this stress (*THEREFORE*). Each of these dimensions is described below (see Fig. 2 also).

WHEN pain creates stress

As pain progressed and became chronic, pain appeared to have an increasingly widespread negative impact on individuals' lives. As participants' lived experience with pain and associated limitations in functioning cumulated, the apprehension of their future with pain was increasingly threatening. The recurring deceptions and obstacles associated with pain and its management influenced the meaning participants attributed to pain. Daily pain experiences were thus grounded in both past experiences and anticipated evolution of their pain in the future.

Changes in symptoms

The changes individuals have noticed in their pain experience since its onset led to increased apprehension of the future. The changes in their symptoms has been uncertain and often perceived as a source of stress.

“I said if I’m like this when I’m 47, then where will I be when I’m 80?

Where will I be when I’m 60? Where will I be next week? This is killing me!” (Spruce tree, 47 y.o., 21 years living with pain, focus group 4)

Continuing lack of medical innovation

Repeated medical encounters in the context of pain chronicity were often difficult for individuals as they were a constant reminder of their powerlessness in treating their pain condition. As time went by the impact of this lack of treatment innovation became increasingly burdensome.

“That way, going to see my doctors, even if it’s just once a year and I like them... My family doctor had been following me for 35 years, it’s getting... I don’t want to go anymore, it’s getting just too depressing. It’s too much for me to, to have it in my face. I’ve got nothing to offer you...” (Owl, 50 y.o., 6 years living with pain, focus group 2)

Wear and tear: between hope and deception

The longer individuals had been trying to find solutions for their pain, the more they exposed themselves to possible deceptions. There seemed to be a fragile equilibrium between hoping that one’s pain condition will be cured and exposing oneself to repeated disappointments of failed treatment attempts.

“It wears you out, constantly trying things. How many times, you know, sometimes on Facebook... Ah, a new treatment, they’ve discovered something new that, you know, will solve it. And you think, well maybe... So it gives you some hope, and then afterwards, you go from despair to hope, to disappointment, to...” (Hummingbird, 44 y.o., 23 years living with pain, focus group 2)

WHY pain creates stress

In the context of pain chronicity, individuals attempted to make sense of their world and redefine who they are. As such, the threat associated with chronic pain became amplified and led to significant changes in individuals’ perceptions of themselves. Their physical and social needs were often described as incompatible, leading to difficult choices to make as they navigated their life with pain. The constant evolution of symptoms also led to changes in their appraisal of pain, its experience and their reactions to it. As described earlier, how stressful pain was perceived was

very subjective and depended in part on what was the most important for participants at that moment.

Incompatible physical and social dimensions: Managing pain vs. social life

Many participants described that they often found themselves having to manage incompatible aspects of their life and social expectations. Some participants described how they have to hide their pain) from others as not to push others away. However while this can be seen as a way to maintain a social life, the cost of such strategy is having to deal with increased pain.

“When you’ve been in pain ever since you were young, you learn to hide it, you learn to... have, be, how can I say it... Like pain, I show nothing. You go about your business, even if you know that by the time you get home it’ll be like... You’ll go to bed because you just can’t do anything anymore. But hey, it’s okay .” (Cricket, 56 y. o., 45 years living with pain, focus group 5)

For others, the need to protect social meaningful relationships and social roles even if this means dealing with increased pain was a thoughtfully weighted decision. Nonetheless, balancing these incompatible dimensions of their daily living was seen as stressful.

“Oh no, I can’t keep myself from going out because of it. For me, that would be... I don’t know. My social life is so important to me, that I think to myself, who cares, ‘It hurts, it hurts,’ you know. But it’s a drag, it’s stressful. But I think to myself, ‘If it keeps me from living, well that’s another matter.’ I won’t keep myself from living my life because I’m in pain.” (Venus, 62 y.o., 37 years living with pain, focus group 1)”

Finding the optimal balance between pain suppression/pain management and the ability to engage in life in a meaningful way was also identified as a challenge by many participants. This preoccupation might be associated with undesirable side effects of risks associated with pain killers such as opioids.

“She doesn't want to increase my dose of Dilaudid, either. I mean, I don't want to be stoned all the time, either! You know what I mean, that's... there's that, too.” (*Venus, 62 y.o., 37 years living with pain, focus group 1*)

Loss of identity

With the chronicity of pain and associated limitations in functioning, individuals' sense of self and identity was often threatened, whether it was at the physical or social levels.

“You know, no, pain is not who I am, but it's part of my life and it's... it's affecting everything else. My relationships with others, my couple, my relationships with my children, with everything...

For sure it's stressing me out, because in the end... [hesitation] I have aspirations in life, and my body doesn't allow me to do what I'd like, so I'm always falling short on... on satisfaction, that's for sure.”

(*Hummingbird, 44 y.o., 23 years living with pain, focus group 2*)

HOW pain creates stress

Individuals do not live in hermetic vases; they are an integral part of multiple psychological, social and cultural systems. It is through their interactions with these different systems that the stressful characteristics of chronic pain were amplified.

The pain experience not taken seriously

Pain is, by definition, a subjective experience for which no objective test exists. This places individuals in precarious situations related to their own and others' acceptance of their condition. The invisibility of their pain as well as the lack of knowledge in many medical communities and participants' social circles more broadly made it difficult for participants to live with pain on a daily basis.

“Yeah, and the weight of the years and the baggage of... whether it's the diagnoses or the doctors, who're telling us: 'It's all in your head.' There's a part of that weight that you can shed as you go along, but you can't get rid of it all. It gets heavier and heavier.” (Bumblebee, 56 y.o., 50 years living with pain, focus group 5)

Many participants noticed a change in the extent to which others understood their pain condition as time went by. Initially participants' felt others understood what was perceived as *temporary* limitations. However, as time went by individuals reported that other's comprehension about their special situation eroded and this was perceived as an attack to the legitimacy of their experience. Participants might be struggling to explain the lack of treatment response for their chronic pain to others who expect a cure.

“People don't understand the pain. Here's an example: my boyfriend sometimes sees me in the morning with a warm pillow or an ice pack, and says, 'It's back.' He asks, just a question, 'What, it hurts again?' It's been years and years that I've had this pain. This means that he doesn't really understand what chronic pain is. I'm not going to spend my time complaining. That's why when it's not... not visible, I think it's harder.

People don't understand it as much." (Apple tree, 66 y.o., 21 years living with pain, focus group 4)

Meaning given to the pain

Individuals talked about the importance for them and others to understand what had been happening to their body but also more broadly to themselves as a person. Often they were unable to find the answers they were looking for, or an explanation for their pain. This unknown was identified as an important source of stress and frustration for many.

"Well, not at all because sometimes I've... and I experienced... Once I saw a doctor who said, 'Listen, I understand you, I believe you, but I'm...' He admitted that he didn't know. There was nothing there. We tried several things, and he said, 'For more than that, it'll require an autopsy.'" (Hummingbird, 44 y.o., 23 years living with pain, focus group 2)

This difficulty in making sense of their experience in the absence of a diagnosis could make it more difficult to explain or communicate their pain to others.

"What shocks me the most is when someone tells me... A guy my weight, my height, says, 'You look alright, what can you do? Can you do something else?' I say, 'Come and sit down, let's talk about it.' And people can't even imagine it. Chronic pain can't be explained, you have to experience it." (Ruby, 77 y.o., 21 years living with pain, focus group 3)

Expectations and social roles

The loss of identity associated with pain was in part attributed to being unable to engage in life according to what was most valued in society. These expectations and social roles that individuals were no longer able to meet weighted heavily on individuals' shoulders.

“But in life, you know you succeed when you’ve got control, you’ve got your work, your family under control. You take care of your business, you perform. Then you’re in control, and you’re valued by society. I’m no longer valued by society because I no longer have the same abilities, even if I’m in full control of my faculties.” (*Owl, 50 y.o., 6 years living with pain, focus group 2*)

THEREFORE

In the context of stress related to pain, individuals engaged in strategies in order to escape, minimize, or gain perceived control over pain and stress.

Avoidance and isolation

In response to pain-related stress, individuals sometimes resorted to avoidance strategies and isolation to minimize the impact of contextual factors on their pain experience.

“I stay at home, and I don’t see anyone. I lock myself in. I stress less over my pain, because I live with it alone (several people validate it). I don’t need to worry about it, ‘Do I look like I’m in a good mood or not,’ you know.” (*Neptune, 41 y.o., 26 years living with pain, focus group 1*)

Giving up

Another approach to manage pain-related stress was to let go of the things that are no longer in their hands and as such adapt to the chronicity of their experience.

“I used to worry a lot about what other people thought, but then I realized that it wasn’t worth it, because they’re going to think what they want anyway. It doesn’t matter what I think. So I can’t control what they’re going to think, but I can control what I think. So I’ve decided to do a little

bit of ‘I don’t care.’ Just a little bit, because people are going to think something anyway.” (Birch tree, 47 y.o., 26 years living with pain, focus group 4)

Focus on coping strategies

Individuals described a helpful process of letting go of the things they did not have control over to focus on things they could do to help their daily experience of living with pain.

“It’s still a positive control, that we can take measures that will help us, too, whether it works for some people or not. But I see it as a... We’ve got this control. We don’t have it over the pain, but we can do things to help ourselves.” (Topaz, 55 y.o., 12 years living with pain, focus group 3)

Personifying the pain

When individuals faced recurrent lack of control and unpredictability of pain, where there was no logic to their pain, some of them reacted by perceiving pain as a separate entity from themselves.

“[The pain is] hard to control without tools, with tools like these. For me it’s like coming to get some tools. It becomes a little bit more manageable. I won’t say it too loud, just in case my pain hears me (laughing).” (Birch tree, 47 y.o., 26 years living with pain, focus group 4)

Discussion

Grounded in the lived experience of individuals suffering from chronic pain, study results provide preliminary support for key aspects of the Pain-N.U.T.S. framework. Multiple components of the daily pain experience were characterized by the presence of one or more of the N.U.T.S. characteristics. Despite the chronicity of individuals' pain conditions, all four stressful characteristics of pain seemed relevant to the experience of chronic pain.

While there was overlap in what participants described as novel and unpredictable, these dimensions seemed nonetheless distinct. Often, a new situation is also unpredictable. However, unpredictability of a situation is often grounded in previous experiences and one's inability to make a confident prediction of an outcome. Novelty on the other hand is sometimes predictable but nonetheless stressful (e.g., receiving a new diagnosis).

Consistent with the larger stress literature, there was noticeable inter-individual variations in what was perceived as stressful. These inter-individual differences in what was experienced as stressful reflect well the subjective nature of stress.

Beyond the inherent stressful characteristics of their pain experience (e.g., unpredictable pain intensity), contextual factors seemed to amplify the impact of the N.U.T.S. characteristics on pain appraisal. Indeed, the experience of pain, when chronic, is embedded in larger individual, familial and systemic influences which contribute to how stressful this experience is. Many of these contributors were associated indirectly with the duration of pain, leading to an accumulation of stress-related burden. This is in some ways consistent with the concept of allostasis. Allostasis refers to the body's ability to adapt to stress or pain through regulation of internal resources and maintaining stability (3). The prolonged presence of either or both stress or pain leads to a system overload that deregulates this internal balance. Indeed, when pain is chronic, there is often a

dysregulation of the stress response (43, 44). This is consistent with study findings; participants expressed a heavier weight of pain-related stress (wear and tear) as multiple losses and deception cumulated; this in turn seemed to negatively impact pain experience.

The two-tiered Pain-N.U.T.S. framework shares similarities with Lazarus and Folkman's transactional stress model (45, 46) in which stress is described as an evolving cognitive and behavioral attempt to manage external or internal demands that one has appraised as taxing or requiring greater resources than what is available. Primary appraisal would refer to a situation perceived as a threat, a challenge or irrelevant based on situational and individual characteristics. Secondary appraisal then refers to the cognitive processes, beliefs and sense of efficacy in facing the situation. Applied to this study's results, the N.U.T.S. characteristics seem to influence primary appraisal of pain as a threat, challenge or being irrelevant.

Secondary appraisal typically refers to one's cognitions and beliefs associated with the presence of pain, such as pain catastrophizing. Study results however suggest that secondary appraisal, thus one's psychological response to pain, is in part influenced by the presence of the N.U.T.S. characteristics in their pain experience. Indeed, many participants reported that the experience of pain-related stress was negatively impacting mood and emotions. The association between stressful characteristics of pain and psychological responses to pain has been individually recognized in previous studies. For example, research has suggested that fear-based responses to pain could be grounded in the unpredictable nature of one's pain or lack of control over the pain experience (47). Social isolation could be present in response to pain as a threat to the ego (21). Even more elaborate models such as the Fear-Avoidance Model of Chronic Pain (48-50) could be seen as transversal to the Pain-N.U.T.S. framework where patients might enter the vicious cycle of pain avoidance to minimize one or another stressful characteristic of pain. As such, it appears

relevant and important to examine one's cognitive and behavioral responses within its context of occurrence, namely by considering the stressful characteristics of the pain experience that might be feeding into these psychological responses.

It is also important to note that individuals changed their perception of what is interpreted as stressful over time. The in-the-moment experiences of pain seemed embedded in broader contextual factors that consider previous experiences and identities, current struggles, and concerns about the future and evolution of symptoms. Participants were able to reflect on the evolution of their pain appraisal over time, learning from past experiences to either experience increased or decreased apprehension of subsequent experiences. Some of the N.U.T.S. characteristics were embedded in participants' memories and as such these past experiences interacted with current stress-related characteristics to influence pain appraisal. There is indeed evidence to suggest that stress could contribute to the activation of pain-related fears and thus influencing subsequent behavioral reactions to future pain episodes (17, 51).

The presence of chronic pain seemed to force individuals to balance multiple risk roles. Indeed, participants described that pain often threatened their sense of self, identity, legitimacy of their experience, and abilities to fulfill their different social roles. It appeared difficult for participants to navigate these different challenges which reinforced the perception that risks were omnipresent and often unavoidable. This is similar to the notion of embodied risks described by Eaves and colleagues (52) who interviewed individuals living with temporomandibular disorders. In their study, they described that patients are living in a state of embodied risks, feeling constantly vulnerable to symptom flare-ups. They noted that risks are omnipresent, including physical risk (pain), social risk (avoiding meaningful social interactions to reduce pain), and threatened legitimacy (forming self-identities while coping with uncertain pain evolution). From this

perspective, every gain made (for example, choosing to stay home to maintain pain at a manageable level) is also associated with a loss (social isolation). This constant state of juggling with multiple risks simultaneously contributed to the chronicity of their stress experiences and responses.

Participants do not stay passive in front of pain-related stress and engage in multiple, sometimes creative (such as superstition), strategies to limit or reduce its impact in their daily life. While some participants described trying to focus on behaviors or problems over which they had control (pacing strategies) and letting go of elements that were out of their control (judgment of others), other participants seemed to put significant amount of efforts in avoiding situations that could lead to the experience of one or more N.U.T.S. characteristics. The concept of habituation, conceptualized as one of three cognitive processes aimed at resolving uncertainty [along with attention and learning (53)], seemed to develop as participants were exposed over time to repeated pain-related stress with little control over their experience. Deciding to disengage from activities and situations or to stop caring about negative consequences brought on by pain were interpreted as attempts to reduce pain-related stress.

Limitations

Recruitment strategy for this study targeted those who had an interest in discussing the relationship between stress and pain. They were also patients who for the most part had been living with chronic pain for years. While these might not be limitations per se they are important sample characteristics to take into account in the interpretation of study results. The analysis is also based on a limited number of participants, with balanced genders but limited ethnic diversity. In addition, the study goal and methodology did not allow to compare the fit of different stress models applied to the pain experience. While we explicitly elicited criticisms of the model from participants and

examples of experiences that did not fit stressful experiences of their pain, it would be interesting for future work to examine through an integrative lens the different stress models that exist in order to further our understanding of stressful characteristics of pain. Finally, while not a limitation per se, participants described in detail the vicious cycles present between pain and stress. Many mentioned that increases in stress (related or not to their pain) led to an increased pain intensity and decreased functioning. The present analysis focused on exploring the ways in which the pain experience is stressful; additional research would be needed to better understand how stress itself can also influence the pain experience.

Implications

The N.U.T.S. characteristics seem to offer a comprehensive framework to understand characteristics of pain itself that might trigger a physiological stress response and fuel the bidirectional stress-pain relation. This project will serve as the foundation for subsequent studies that will examine the Pain-N.U.T.S. framework within brain systems known to be involved in both pain and stress experiences (2, 54).

From a clinical perspective, better characterization of stressful characteristics of pain might help identify untapped needs. Often, psychological interventions will target secondary pain appraisal [e.g., cognitive processing (such as pain catastrophizing), beliefs and efficacy], without paying attention to individual factors that could influence primary appraisal of pain (whether pain is interpreted as a threat, a challenge, or as irrelevant). The role of psychological responses to pain (secondary appraisal) must thus be examined and addressed within the context of the pain experienced (primary appraisal), namely its level of stressfulness. Being able to break down the pain-related stress into its specific components (N.U.T.S.) might be a first step to reduce fear related to the pain experience by helping patients better understand it. Indeed, research has shown

that when individuals learn to break down their stress experience into its individual N.U.T.S. components, it leads to decreased physiological responses to stress (10). Such approach could be adapted and tested for chronic pain populations. It could be an interesting therapeutic target independent or combined with individuals' psychological responses to pain.

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Figure legends





Figure 1. Central layer of analysis related to the N.U.T.S. framework. Six aspects of pain emerged as influencing appraisal of pain as stressful, namely pain intensity, pain location and quality, duration of pain episodes, functional limitations, management and treatment, and diagnosis. The presence of  Novelty,  Unpredictability,  Threat to the ego, and  Sense of low control are reported.

Figure 2. Second layer of analysis. Beyond the inherent stressful characteristics of pain (central elements of the N.U.T.S. framework), contextual elements related to the chronicity of pain can influence pain-related stress experiences and their appraisal. This includes elements related to the persistence over time of pain, including how symptoms evolve over time, the impact of repeated treatment failures and the wear and tear associated with sustained pain experience [WHEN]. Other elements pertained to the amplification of sensory and emotional aspects of the pain experience as it persists, including shifts in perception of pain-related threat, ongoing competition between different individual and social needs, and loss of identity [WHY]. Individual and systemic influences of pain experience explained in part why the chronicity of pain adds to its degree of stressfulness, namely when pain is invalidated, meaning and interpretation of pain experience are unstable, and when expectation and social roles are impaired [HOW]. Last, these stressful characteristics lead participants to try to protect themselves from this stress [THEREFORE].

Table 1. Demographic characteristics of patients who participated in the focus groups

	FG 1	FG 2	FG 3	FG 4	FG 5	FG 6	TOTAL
N	8	8	6	8	7	4	41
Age in years (median (range))	44 (38-70)	58 (44-77)	56 (49-77)	52 (34-66)	56 (44-70)	59 (32-78)	57 (32-78)
Sex (N)							
Female	4	6	2	6	6	1	25
Male	4	2	4	2	2	3	17
Gender (N)							
Female	4	6	2	6	6	1	25
Male	4	2	2	2	2	2	14
Undifferentiated	0	0	1	0	0	0	1
Missing	0	0	1	0	0	1	2
Education level (N)							
High school	0	1	0	3	0	1	5
College	5	2	3	2	3	0	15
University	3	5	3	3	4	3	21
Pain duration range (years)	1-38	6-52	2-21	3-26	2-50	5-34	1-52
Pain intensity (0-10) (median (range))	7 (6-8)	6.5 (4-8)	6 (5-8)	6.5 (6-9)	6.5 (5-9)	6.5 (5-7)	6 (4-9)
Pain location (N)							
Diffuse body pain	7	7	1	4	5	4	28
Upper body pain	0	1	1	4	2	0	8
Lower body pain	1	0	3	0	0	0	4
Back pain	0	0	1	0	0	0	1
Type of ongoing pain care (N)	4	5	4	2	1	2	18

Primary care (family medicine)	3	1	1	1	3	2	11
Secondary or tertiary multidisciplinary pain centers	0	0	1	4	1	0	6
Specialist	1	2	0	1	2	0	6
None							

Stressful characteristics of pain

Pain intensity U T S

Pain location & quality N U T

Duration of pain flares U S

Functional limitations N U T S

Management/treatment N U T S

Diagnosis N U T

WHEN pain creates stress

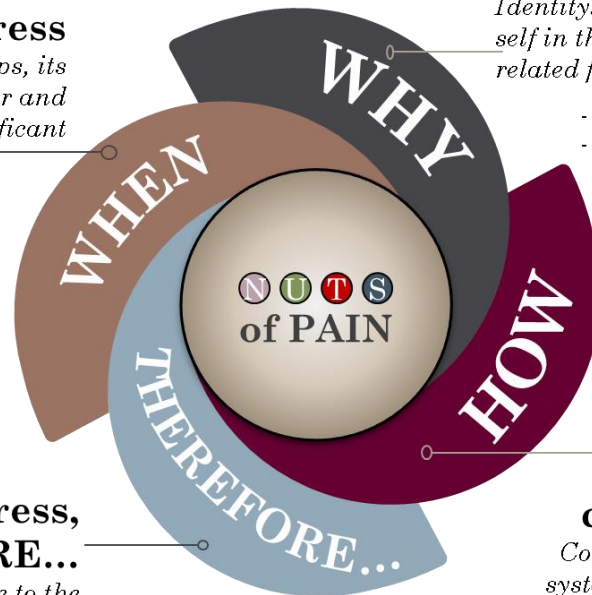
Effect of time: As pain develops, its consequences become broader and more significant

- Changes in symptoms
- Continuing lack of medical innovation
- Wear and tear

WHY pain creates stress

Identity: Defining one's sense of self in the context of pain and related functional limitations

- Incompatible dimensions
- Loss of identity



Pain creates stress, THEREFORE...

Reactions to pain: in response to the stress, strategies are used to minimize its impact

- Avoidance and isolation
- Giving up
- Focus on coping strategies
- Personifying the pain

HOW pain creates stress

Context: individual and systemic influences of the pain experience can amplify pain-related stress and affect its appraisal

- The pain experience not taken seriously
- Meaning given to the pain
- Expectations and social roles