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ORIGINAL RESEARCH

The Experience Sampling Method in Small Fiber Neuropathy: The Influence of Psychosocial Factors on Pain Intensity and Physical Activity

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Purpose: Small fiber neuropathy (SFN) is characterized by neuropathic pain, associated with decreased quality of life (QOL). It remains unclear which psychosocial factors play a role in SFN. The experience sampling method (ESM) allows a profound understanding of the real-time fluctuations in reaction to events. The main goal of this study was to increase knowledge of the interrelationships between pain intensity, physical activity, and psychosocial factors in patients with SFN in daily practice over time.

Patients and Methods: A prospective observational ESM study with the PsyMate© application (smart-eHealth GmbH, Luxembourg) was conducted at the Adelante location of Maastricht University Medical Center+ in the Netherlands. Participants with idiopathic SFN, older than 18 years, with an indication for rehabilitation, were included. Pain intensity, fatigue, positive and negative affect, physical activity, avoidance behavior, and pain catastrophic thoughts were incorporated into the ESM questions. Participants received 10 beep signals per day followed by the above-mentioned questions, for consecutive 7 days. The results were analyzed with linear mixed-effect models.

Results: Twenty-one participants were included with a mean age of 48.24 (SD ± 13.89) years, of whom 76.2% were female. More pain (now) resulted in more physical activity (later) (a) and more physical activity (now) resulted in more pain (later) (b). The first association (a) is influenced by pain catastrophic thoughts and fatigue, and the second (b) by an increase in affective states and a lower level of avoidance behavior.

Conclusion: In idiopathic SFN, pain intensity, and physical activity showed a 2-sided association, influenced by catastrophic thoughts, fatigue, affective states, and avoidance behavior.

Keywords: chronic pain, rehabilitation therapy, biopsychosocial factors, small fiber neuropathy

Introduction

Small fiber neuropathy (SFN) is a chronic neuropathic pain condition, due to damage to the small nerve fibers.[1] Current (pharmacological) pain treatment is mostly insufficient with a lot of side effects and decreased quality of life (QOL).[2,3] More understanding of SFN is necessary to develop a personalized and effective treatment modality that helps patients increase QOL.[4–8] Chronic pain has a great impact on physical functioning and QOL.[8–10] The reverse, influence of physical functioning on the pain experience is also established.[11,12] The exact coherency of pain and physical functioning in SFN has not been clarified.

Pain fluctuates over time and days and is influenced by psychosocial factors such as pain catastrophizing, physical functioning, depression, anxiety, fatigue, and pain-related fear, as observed in several chronic pain conditions.[13–32] These

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psychosocial factors also influence physical functioning, and the development of pain-related disability.[13–30] The hypothesis that pain intensity will result in a decrease in physical functioning, and vice versa is explained by the fear-avoidance model which states that an activity might be interpreted as extremely painful or harmful, resulting in fear of more pain or harm which on its turn can lead to the avoidance of activities.[33,34] On the other hand, not every chronic pain patient will develop a pain-related disability.[35–37]

The assessment of psychosocial factors and pain usually occurs with once or twice-completed questionnaires to compare the outcome measurements and to gather a summative overview of (past) complaints.[38–40] The retrospective character of this kind of assessments is disadvantageous and persistently influences the outcome measurements due to recall and memory bias.[38,39,41–48] Recall bias is the inaccurate remembrance of past events or experiences, and memory bias is the alteration of memory.[49] Both will lead to the remembrance of more intense complaints and negative memories.[38,39,41–48] Nonetheless, a more accurate and real-life assessment exists to avoid these types of bias.[50] Collecting real-life assessments and dynamics is possible with the experience sampling method (ESM), which is a smartphone-based application with repeated measurements in the natural environment.[51–55] A deeper and more reliable understanding of dynamic processes and disease-related fluctuations can be observed, especially, the variability of symptomatology and pain intensity,[38,51,56,57] avoiding memory and recall bias.[50] ESM is labeled as a reliable and valid tool to assess daily life fluctuations and dynamics in chronic pain disorders.[32,38,39] These momentary assessments can be important for patients and caregivers to understand and be aware of the fluctuations of complaints over time.[32,58]

The relation between physical activity and pain and the influence of aforementioned psychosocial factors is not clear yet in SFN. For this reason, we conducted a prospective observational ESM study that aimed to gain more information on the patterns of pain intensity and physical activity in SFN. These insights may clarify the dynamics of psychosocial factors with pain intensity and physical activity in patients with SFN.

Material and Methods

Study Design

A prospective, observational study with ESM was conducted at the rehabilitation department of Adelante location of Maastricht University Medical Center+ in the Netherlands. The study was approved by the medical ethical committee of Zuyderland Medical Center (METCZ20210022). This study complies with the Declaration of Helsinki.

Study Population

The Department of Neurology of the Maastricht University Medical Center+ is a tertiary referral center for diagnosing SFN and treatment advice. Participants were recruited between September 2021 and March 2022. Through an online advertisement, potential participants were informed and could approach the research team. The research team contacted possible participants by phone to check the in- and exclusion criteria, after getting permission to check their electronic patient file. Potential participants were then referred to the Department of Rehabilitation Medicine. Interested participants of the outpatient neurological clinic were also referred to the Department of Rehabilitation Medicine to be screened by the rehabilitation physician. The inclusion criteria were diagnosed with idiopathic SFN according to the Besta criteria,[59] age 18 years or older, and an indication for rehabilitation treatment (eg, experiencing pain-related disability in daily life). The exclusion criteria were the presence of psychiatric comorbidity and insufficient understanding of the Dutch language to fill in ESM and questionnaires. When the physician and participants approved, enrollment in the study started. A research assistant contacted participants for further information about the study and to give information about the smartphone application PsyMate©. All patients provided informed consent. Then, baseline characteristics, such as SFN diagnostics, were retrieved from the electronic patients' files. Figure 1 shows the study flowchart.

ESM

Repeated measurements were assessed with the PsyMate© application (smart-eHealth GmbH, Luxembourg). PsyMate© is an application on the smartphone, compatible with Android and iOS, which can be easily downloaded. We used PsyMate© to gain more information about pain intensity, physical activity, and potential psychosocial factors, such as positive and negative affect, pain catastrophizing, fear avoidance beliefs, and avoidance behavior of participants with SFN.

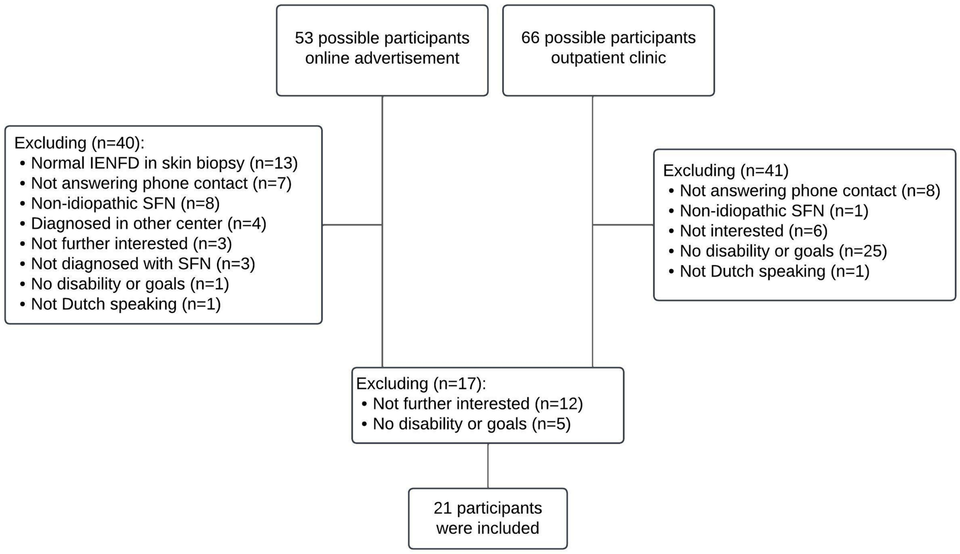

Figure 1 Study flowchart. 119 possible participants were approached, of whom 81 participants were excluded by the research team due to several reasons. In a second step, a rehabilitation physician invited 38 potential participants for a consultation to inform patients about rehabilitation treatment possibilities and check the indication for treatment. With this additional information, 17 persons refrained from treatment. At the end, 21 participants were included.
Abbreviations: IENFD, intra-epidermal nerve fiber density; SFN, small fiber neuropathy.

PsyMate© was programmed to generate 10 beep signals a day between 7:30 AM and 10:30 PM, for 7 consecutive days.[54] A random schedule, with a minimum interval of 15 minutes and a maximum interval of 90 minutes between two beeps, was set. After each beep signal, around 14 short questions and statements appeared. Participants had 15 minutes to fill out each question and statement, otherwise, it disappeared. A couple of statements are original, adopted from PsyMate©, and other statements were added by our research group, see Table 1.[60] All questions, except for pain and fatigue, could be answered on a 7-point Likert scale (1: not at all, 7: very much), which is the standardized answer option in PsyMate©. Questions about pain and fatigue consisted of an 11-point numeric rating scale because both questions have been taken over from the standardized pain and fatigue questionnaires. All questions in PsyMate© have adequate psychometric properties to measure change over time.[61] The following questions had open-ended answer options "What am I doing?", "Where am I?", and "Who is joining me?". Table 1 provides an overview of all ESM questions.

Table 1 Overview of ESM Questions with Scoring

ESM Question	Score	Original or Self-Designed Statements
Pain intensity		
I am in pain	0 = no pain, 10 = worst pain	Original
Fatigue		
I am tired	0 = not tired, 10 = very tired	Original
Affect		
I am cheerful	1 = not, 7 = very	Original
I am relaxed	1 = not, 7 = very	Original
I am sad	1 = not, 7 = very	Original
I am anxious	1 = not, 7 = very	Original

(*Continued*)

Table 1 (Continued).

ESM Question	Score	Original or Self-Designed Statements
Physical activity		
I was physical active since the last beep signal	1 = not, 7 = very	Additional
Pain catastrophizing		
I want the pain to stop	1 = not, 7 = very	Additional
I am not thinking clear	1 = not, 7 = very	Additional
Pain thoughts and beliefs		
I try to move less	1 = not, 7 = very	Additional
The pain determines what I am doing	1 = not, 7 = very	Additional
General open questions		
What am I doing?	Work, housekeeping-related activities, food-related activities, selfcare, care for others, resting, social contact, nothing, use of social media, sports, relaxing, something else.	Original
Where am I?	Home, visitation, at work, public place, on my way to, somewhere else.	Original
Who is joining me?	No one, partner, family, friends, coworkers, acquaintances, strangers.	Original

Within the standardized procedure prior to the rehabilitation physician visit, a set of questionnaires was completed including Pain Catastrophizing Scale (PCS), Hospital Anxiety and Depression Scale (HADS), SF-12, and SFN-specific questionnaires: SFN-RODS (SFN-specific Rasch built Overall Disability Scale) and SFN-SIQ (SFN - Symptom Inventory Questionnaire.[62] The PCS questionnaire inventories the presence of catastrophic thoughts about pain with 13 questions. A score higher than 30 indicates the presence of catastrophic thoughts.[60] HADS questionnaire is used to measure depressive and anxious symptoms.[63] The questionnaire is divided into two subscales, with each 7 items, related to either anxiety or depression, with the following scores: "normal" between 0 and 7, "mild" between 8 and 10, and "moderate" higher than 11.[64] The highest score on the subscale is 21. The SF-12 questionnaire is estimating the health status with 8 items.[65] The outcome ranges between 0 and 100, in which a higher score than 50 indicates better physical and mental health functioning than the general population.[66] The SFN-RODS is a 32-item questionnaire, measuring the ability in daily life activities in patients with SFN.[67] Three different answer options are available. The total score ranges between 0 and 100. A higher score indicates more disability. The SFN-SIQ is a 13-item SFN-related questionnaire, measuring mainly the autonomic complaints in SFN.[67] Four different answer options are available. The total score ranges between 0 and 100, in which a higher score indicates more autonomic complaints. All mentioned questionnaires are valid and reliable.[60,65,67,68] Questionnaires were filled in before installing the ESM application.

All included patients were diagnosed with SFN according to the Besta criteria: the combination of at least two clinical signs and symptoms, abnormal temperature thresholds in quantitative sensory testing (QST), and/or reduced intra-epidermal nerve fiber density (IENFD) in skin biopsy, with no involvement of large fibers.[59,69]

Statistical Analysis

Baseline characteristics were calculated with descriptive statistics. The categorical variables were calculated as frequencies and proportions. Continuous or dichotomous variables were calculated as means and standard deviation. Normality assumptions were checked with SPSS (Version 27.0, SPSS Inc., Chicago, IL, USA).

The first aim was to gain more information on the association between pain intensity and physical activity (first direction) and between physical activity and pain intensity (second direction) over time. The ESM data were analyzed with linear mixed-effects models on 3 levels; patients, days, and beeps. In the following steps, the model was built 2-sided (pain intensity vs physical activity, and physical activity vs pain intensity), with random and fixed effects. The relation between pain intensity and physical activity was analyzed with the following variables: "I am in pain" and "I was physically active since the last beep". This is the first model (model 1), see Figure 2.

The second aim was to identify the impact of several psychosocial factors in the association between pain intensity and physical activity (model 1). In order to identify the factors that influence model 1, several additional steps were taken. In the second model (model 2), psychosocial factors including "I am sad", "I am anxious", "I am cheerful", "I am relaxed", "I want the pain to stop", "I can't think clearly", "The pain determines what I am doing", and "I try to move less" were added. In the third model (model 3), baseline variables of baseline characteristics and outcomes of the baseline questionnaires were included. This process is illustrated in Figure 2 and was carried out using a backward stepwise regression analysis. Only statistically significant factors were added to the final model after each step. Both models were analyzed with a time-lagged interval, meaning that pain intensity (now) was linked to physical activity plus or minus 1.5 hours later, and vice versa, as shown in Figure 3. The models were also analyzed with a longer time-lagged interval of plus or minus 3 hours.

Analyses were performed with SPSS (Version 27.0, SPSS Inc., Chicago, IL, USA). A significance level of 0.05 was used.

Results

Baseline Characteristics

In total, 119 possible participants were approached. Eighty-one participants were excluded due to several reasons by the expert team, see Figure 1. Thirty-eight (interested) participants were referred to the rehabilitation physician, of whom 21 were included (see Figure 1). The total study population consisted of 16 females (76.2%), with a mean age of 48.24 ± 13.89 years. More than half of the participants had a partner. In addition, 50% of the participants were unemployed. The outcome of the questionnaires and the baseline characteristics are presented in Table 2.

Some ESM questions had a lower response rate, including "What am I doing?", "Where am I?", and "Who is joining me?". Therefore, these ESM questions could not be included in the analysis.

The Impact of Pain Intensity on Physical Activity (a)

Physical activity influences the pain intensity (p-value = 0.035, 95% CI [0.00–0.14]), indicating an increase of 1 point on physical activity resulted in an increase of 0.07 in pain intensity, see Table 3. In model 3, we accounted for pain catastrophic thoughts ("I want the pain to stop") (p-value < 0.001, 95% CI [0.35–0.54], coefficient 0.45) and fatigue (p-value < 0.001, 95% CI [0.19–0.32], coefficient 0.25). No affective states were statistically significant in this analysis nor did the time-lagged analysis reveal any statistically significant association.

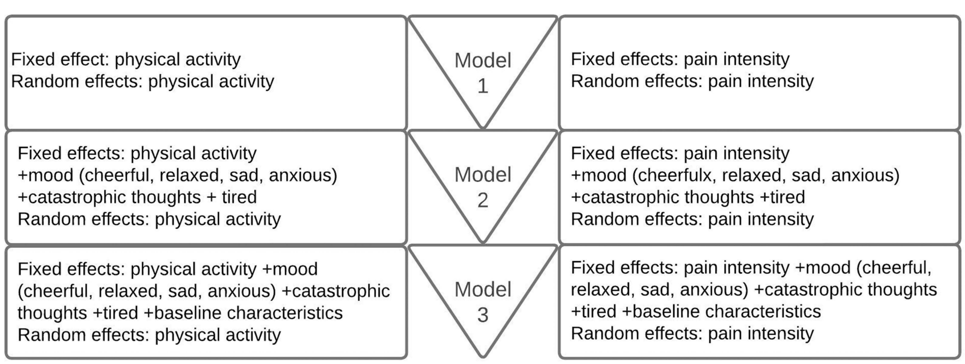

Figure 2 Structure of linear mixed-effects model.

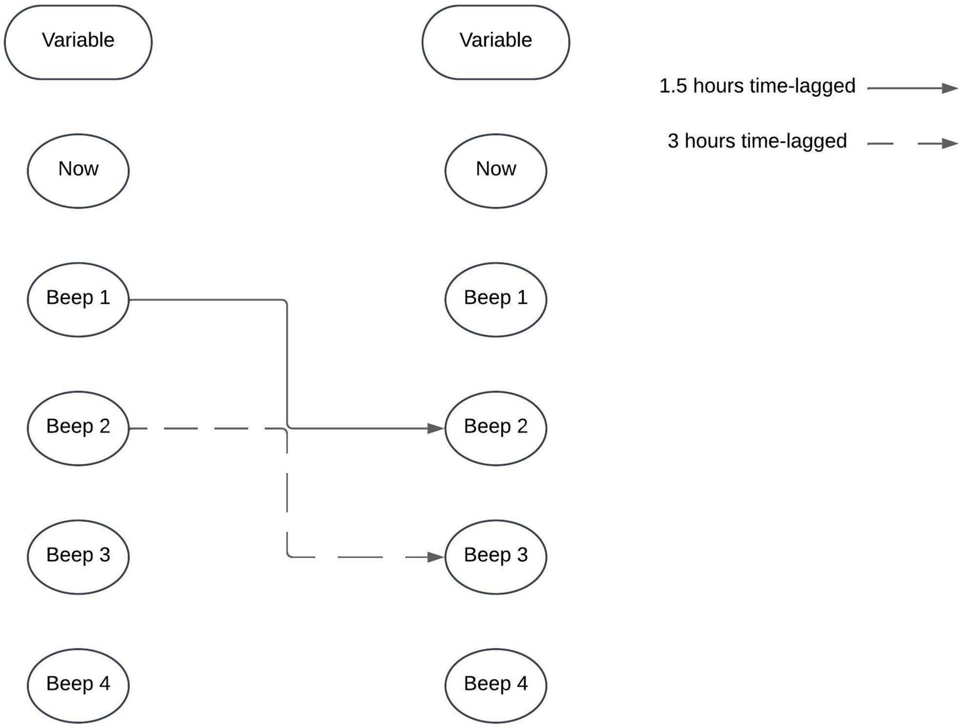

Figure 3 Time-lagged analysis.

The Impact of Physical Activity on Pain Intensity (b)

Pain intensity also influenced physical activity (p-value = 0.029, 95% CI [0.02–0.30]), whereby an increase of 1 point in pain intensity increased the physical activity with 0.16, see Table 4. Model 3 accounted for different moods, such as: cheerful and anxious affective state (p-value < 0.001, 95% CI [0.21–0.51] coefficient 0.36, p-value = 0.045, 95% CI [0.00–0.35] coefficient) 0.17 and avoidance behavior ((“I try to move less”) (p-value = 0.017, 95% CI [−0.24- −0.02] coefficient −0.13). Analyzing physical activity as a time-lagged variable showed no statistically significant association.

Table 2 Patient and Psychosocial Characteristics of Small Fiber Neuropathy Patients (N = 21)

Sociodemographic Characteristics	
	N (%)
Gender, female, n (%)	16 (76.2)
Age in years, mean (SD)	48.24 (13.89)
Marital status, n (%)	
Relationship	14 (66.6)
No relationship	7 (33.4)
Employment, n (%)	
Unemployed	11 (52.4)
Employed (paid)	10 (47.6)

(*Continued*)

Table 2 (Continued).

Sociodemographic Characteristics	
	N (%)
SFN characteristics	
Decreased IENFD in skin biopsy (%)	20 (95.2)
Abnormal QST (%)	14 (66.7)
SFN duration (years)	2.71 (2.80)
Psychosocial characteristics	
PCS, total score, mean (SD)* (0–52)	18.48 (11.90)
HADS, subscale anxiety, mean (SD)^ (0–21)	7.71 (4.44)
HADS, subscale depression, mean (SD)^ (0–21)	7.90 (3.55)
SF-12, subscale general total health[#](0–100)	11.00 (2.17)
SF-12, subscale mental health[#] (0–100)	27.29 (4.43)
SF-12, subscale physical functioning[#] (0–100)	16.29 (3.55)
SFN-RODS, mean (SD)[$] (0–100)	66.18 (16.66)
SFN-SIQ (CM), mean (SD)[+] (0–100)	49.71 (9.12)

Notes: *a higher score indicates more catastrophic thoughts, ^score between 0–7 is normal, 8–10 is borderline, ≥11 is abnormal, [#]a higher score indicates a lower QOL, [$]a higher score indicates more physical disability, [+]a higher score indicates more autonomic complaints.
Abbreviations: n, number; SD, standard deviation; SFN, small fiber neuropathy; IENFD, intra-epidermal nerve fiber density; QST, quantitative sensory testing; PCS, Pain catastrophizing scale; HADS, Hospital anxiety and depression scale; SF-12, short form 12 questions; PIPS, Psychological inflexibility in pain scale; SFN-RODS, SFN specific Rasch-built overall disability scale; SFN-SIQ, SFN specific symptom inventory questionnaire; CM, centile metric.

Table 3 Overview of Model 1 and Model 3 with Associations Between Pain Intensity and Physical Activity

	Model 1 AIC = 1919.06			**Model 3 AIC = 1767.40**		
	Estimate	**95% CI**	**p-value**	**Estimate**	**95% CI**	**p-value**
Intercept	5.31	4.57–6.04	<0.001	2.01	1.23–2.80	<0.001
Physical activity	0.08	0.00–1.17	0.052	0.07	0.00–0.14	0.035
Pain catastrophic thoughts				0.45	0.35–0.54	<0.001
Fatigue				0.25	0.19–0.32	<0.001

Table 4 Overview of Model 1 and Model 3 with Associations Between Physical Activity and Pain Intensity

	Model 1 AIC = 2442.17			**Model 3 AIC = 2421.87**		
	Estimate	**95% CI**	**P-value**	**Estimate**	**95% CI**	**P-value**
Intercept	2.63	1.77–3.49	<0.001	0.96	−0.24–2.16	0.116
Pain intensity	0.13	−0.00–0.28	0.059	0.16	0.02–0.30	0.029
Mood: cheerful				0.36	0.21–0.51	<0.001
Mood: anxious				0.17	0.00–0.35	0.045
Avoidance behavior				−0.13	−0.24 - −0.02	0.017

Discussion

In this study, we used ESM to gain more information on the patterns of pain intensity and physical activity in patients with SFN. We also wanted to identify possible influencing factors on the relationship between pain intensity and physical activity. This is the first study to investigate such patterns in SFN. Results show that pain intensity and physical activity have a 2-sided association, indicating that more pain (now) resulted in more physical activity (later) (a), and more physical activity (now) resulted in more pain (later) (b). The first association (a) is accounted for by pain catastrophic thoughts ("I want the pain to stop") and fatigue. The second association (b) is accounted for by an increase in affective states, including cheerfulness and anxiousness, and a lower level of avoidance behavior ("I try to move less"). The importance of these observations, as well as, the differences between the associations will be discussed.

The Impact of Pain Intensity on Physical Activity, and Related Factors (a)

More pain (now) resulting in more physical activity (later), was a non-expected result. Based on previous studies, it was hypothesized that an increase in pain intensity results in a decrease in physical activity.[70,71] In earlier SFN research, investigators used paper diaries to understand pain dynamics. SFN patients did not report maximum pain during exercise; however, they reported a higher pain at rest, during sleep, and while standing.[9] The impact of psychological factors was not taken into account. It could be that recall bias influenced the pain scores during rest, sleep, and while standing, due to distraction. Earlier SFN research has observed the use of distraction as a method to forget the pain.[10] Scientific evidence shows a significant reduction in pain intensity during distraction.[72,73] The direct relation between pain intensity and physical activity could be different in neuropathic pain, compared to other pain disorders in which the musculoskeletal system is more involved, eg, joint disorders or osteoarthritis.[31,33,74,75] Research on the effectiveness of exercise on neuropathic pain indeed indicated a pain-reducing effect of exercise, as patients had persistent pain for a longer time, they might have learned by experiencing the effect of being active.[76–79]

The association between physical activity and pain intensity was influenced and supported by pain catastrophic thoughts and fatigue. This means that an increase in physical activity leads to an increase in pain catastrophic thoughts and fatigue, which contributes to the increased pain intensity. First, pain catastrophizing has been defined as a heightened negative state of mind, especially in painful circumstances.[17] Pain catastrophic thoughts are almost always present in chronic pain,[80,81] resulting in fluctuations in pain intensity and a decrease in physical activity.[16,18,80,82–86] This is in concordance with the fear-avoidance model.[33,87] Our findings are in line with the pain literature, in which pain catastrophizing has been observed in SFN.[88]

Regarding fatigue, the increase in pain intensity, due to more physical activity, resulted in more fatigue. In this association, the level of pain intensity was correlated with the level of physical activity. Chronic pain seems to be associated with fatigue, which is present in 64% of the chronic pain populations.[89–91] How fatigue develops throughout the day remains unclear. Different reasons are mentioned, first that patients are getting more tired throughout the day due to increased physical activity, and second that patients are mentally tired by thinking all day about their pain.[92] However, we only observed the relation with the increase in pain and physical activity, independent of fatigue.

The Impact of Physical Activity on Pain Intensity, and Related Factors (b)

More physical activity (now) resulted in more pain (later). This is in line with other chronic pain conditions, such as fibromyalgia.[70,93,94] Based on this, patients with chronic pain will eventually set a couple of (daily) restrictions.[33] In painful polyneuropathy, an increase in disability has been observed due to the experienced pain.[7,95] Earlier research described the restrictions of patients with SFN in daily life, resulting in a change in identity and former way of living.[10] The pain increased by 0.07 points on a scale of 0–10. Questions could arise about the clinical relevance of this pain increase. However, it seems that a change in pain intensity, independent of the level, is relevant and noticed by patients. These findings should be taken into account in the future treatment of patients with SFN.

Physical activity and pain intensity were influenced by two affective states, including cheerfulness and anxiety.[96] An increase in physical activity leading to a more cheerful state was also found by other researchers.[97] Cheerfulness could be related to the fact that patients felt able to be (more) physically active contrary to a period before and were able to perform an activity that they like or consider valuable. In contrast, feelings of anxiety were also related to the increase in physical activity. Chronic pain is mostly accompanied by (increased) negative affect, such as anxiety and depressive thoughts, also in SFN.[80,88,98,99] Fear and pain catastrophic thoughts seem to be mediating the association between pain intensity and physical disability.[100] It is plausible that patients experienced pain-related fear due to an increase in physical activity, being anxious for the possible increase in pain intensity that will follow. If a patient would learn to disconnect (or uncouple) the association between physical activity and their pain levels, in order to accept pain and build up committed action.[101] This is more promising than primarily trying to control pain. However, a difference in fear avoidance has been observed between men and women, in which only women were associated with an increase in pain avoidance.[102]

However, avoidance behavior ("I try to move less") decreased in relation to physical activity and pain intensity. Our results suggest that the increase in pain intensity elevated the amount of physical activity, in which avoidance behavior was not present. The fear-avoidance model indicates that in the presence of higher levels of pain, patients who fear an injury or fear an increase in pain will tend to avoid further activities they fear which can lead to a decrease in (daily) activities (f.e. work, sport, household).[33] The difference with other chronic pain disorders could be in the fact that SFN is a neuropathic pain disorder and not a primary musculoskeletal pain disorder. Patients know that they cannot damage muscles or joints by being active, so they would be probably less fear-avoidant. However, patients who do not know this fact will be precautious.[103] In addition, the activity itself has been found to have neuroprotective effects by strengthening neurogenesis and reducing the inflammatory response.[76] As patients learn this during their efforts to cope with their pain, they may not decrease their activity levels when in pain.

The findings of our study are remarkably different from previous chronic (neuropathic) pain studies. The differences and similarities with previous chronic pain research were discussed above. A lot of hypotheses have been developed throughout the years, of which the fear-avoidance is the most used. As described earlier, in chronic pain conditions, pain catastrophizing and pain intensity influence the level of physical activity, inducing disability.[33] In SFN, the opposite has been observed, which is an interesting finding. Why are SFN patients more active when their pain is increasing? Is it due to distraction or may it be due to a different pathophysiological mechanism in which the musculoskeletal system is not directly involved in SFN, therefore resulting in the increase in pain levels at a later moment when activity stops and the positive effects of being active diminish? This is not observed and described in earlier research. Another hypothesis is the gate control theory, in which the pathway of pain throughout small and large fibers toward the spinal cord is described. The small and large fibers function as a gate-controlling mechanism, whereas the large fibers inhibit activity, and the small fibers facilitate activity.[104] It may be hypothesized in SFN that the pain stimulus reaches the spinal cord, however, by activation of endogenous factors due to large fiber activation by exercise pain hyperactivity in the dorsal horn is reduced, and therefore, more repeated stimulation is necessary for the pain stimulus to reach the spinal cord. Maybe, this is the reason why SFN patients increase their physical activity rather than avoid activity. However, when the period of activity ends, inhibition diminishes and pain can flare up. A focus group in SFN revealed similar findings, where patients explained that they have to plan their (physical) activities, so they can take a day off the day after.[10] In polyneuropathy, patients reported an immediate increase in pain intensity after an activity,[105] confirming our findings. Earlier experimental research observed that a painful shock, not related to physical activity, resulted in global fear of everything.[106] However, more extensive research is necessary to establish our findings, in order to offer patients a more suitable treatment approach.

In addition to pain, patients with SFN experience more complaints and obstacles in daily life, suggesting an undertreatment when current treatment options solely focus on pain reduction.[107] If so, would SFN-related disability decrease if patients were adequately treated and educated, including education about the impact of psychosocial factors and contextual factors including physical activity characteristics? In other chronic pain disorders, rehabilitation treatments addressing psychosocial factors resulted in improvements in physical activity.[108–110] Knowing and understanding the dynamics between the psychosocial factors with pain intensity and physical activity is necessary. This knowledge provides a new dimension in future treatment modalities with a personalized treatment approach. The same has been done in other chronic pain conditions, such as painful diabetic neuropathy and complex regional pain syndrome type 1.[109,110] ESM could be used in a clinical setting to gather information before treatment starts, and patients have their actual appointment with the clinician. This information could guide the clinician in understanding the personal dynamics of pain intensity and physical activity that can be integrated into personalized pain education. However, ESM could also be used in a treatment setting to monitor the effectiveness of a treatment modality throughout time, avoiding memory and recall bias.[111,112] ESM is widely used as a therapeutic monitoring device, especially in mental health disorders.[112] Moreover, ESM could give patients insights into their own disease-related fluctuations. With self-monitoring and self-insight, a more efficacious treatment outcome could be obtained.[111,113]

This is the first study investigating the patterns and complexity of pain intensity and physical activity with disease-related symptoms in SFN. Moreover, the statements and questions of ESM have been extensively validated in different kinds of chronic pain conditions.[53] This ensures the validity and reproducibility of ESM in primary and secondary chronic pain conditions. Another strength is the study design. Repeated measurements allow a more reliable and deeper understanding of disease-related fluctuations and symptoms contrary to traditional questionnaires.[53,56] However, the results may not be applicable to a wider population of neuropathic and musculoskeletal pain but only to patients with SFN. There are also some limitations. The sample size is small with an unequal division of male-female. However, chronic pain and SFN are more common in females. The small sample size could result in selection bias. However, due to multilevel analysis with the repeated measurements a possible bias is prevented. In ESM, calculating a power analysis for the sample size is difficult and still investigated.[114] The aim of this study was also not to search for causality but to gain more information on the patterns of pain intensity and physical activity in SFN and to identify possible influencing factors and relationships in the patient's environment.

Conclusion

In conclusion, we found that pain intensity and physical activity are associated in a bidirectional manner. Catastrophic thoughts ("I want the pain to stop") and fatigue influence the impact of pain intensity on physical activity. Affective states, including cheerfulness and anxiousness, and avoidance behavior ("I try to move less") influence the impact of physical activity on pain intensity. These influencing factors may be targets for personalized treatment of SFN in the future. ESM allows us to understand the dynamics between environment, behavior, and affective state with disease-related symptoms.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, AD, upon reasonable request.

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Disclosure

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