Nexus, uncovered: on the relations between expectancy, avoidance, and somatic sensations

Nadinda, P.G.

1

CHAPTER 1

General Introduction

Our body is made up of complex systems that interact to keep us alive. It is equipped with bodily signals that tell us what we need and when we are in danger. Pain and itch for example, signal that there is potential damage or threat occurring in the body due to internal or external stimuli that urge the individual to act (Liu & Ji, 2013; Raja et al., 2020; Ross, 2011; Wall, 1979). Other sensations, like fatigue, can signal that our body needs rest and sustenance (Boullosa & Nakamura, 2013; Noakes, 2012). These bodily sensations are necessary to protect the body from impending harm by letting us know what cues should be avoided and what cues could be approached (Lenaert et al., 2018; Walters & Williams, 2019). But what happens when these bodily signals prolong? Imagine a car alarm that turns on at the slightest touch, or a smoke detector that cannot be turned off even after the fire has been extinguished. How would we know when to react? How would we know that we are no longer in danger?

Between 10 – 20% of people worldwide (even in childhood) experience chronic somatic symptoms (Petersen et al., 2014; Rasmussen et al., 2020; Vesterling et al., 2023) which are somatic sensations that occur for an extended period of time and therefore affects daily functioning. A notable example of a chronic somatic symptom is chronic pain, which is defined by the International Association for the Study of Pain as pain that lasts for at least three months in duration (Treede et al., 2019). It is often associated with psychological suffering and has been shown to be one of the largest causes of economic burden and disability worldwide (Cohen et al., 2021; Phillips, 2009). Similarly, chronic itch, defined as itch that persists for at least six weeks (Stander et al., 2007) is often associated with persistent scratching which, especially when coupled with a chronic (visible) skin condition, may cause stigmatization (Silverberg et al., 2018). Furthermore, the presence of chronic somatic symptoms, like chronic pain, chronic itch, as well as chronic fatigue, can also impact sleep (Eccles & Davies, 2021; Racine et al., 2016) and especially affect daily functioning as it leads to avoidance of activities that would trigger (the amplification of) somatic sensations (Cole et al., 2021; Gerbershagen et al., 2002; Van Heck & de Vries, 2002). As chronic somatic symptoms can greatly interfere with daily life, it is imperative that the causes and mechanisms behind chronic somatic symptoms are identified.

For many years, there has been a large focus on finding a single cause to the development of chronic somatic symptoms, but it has become increasingly clear that a single cause cannot always be ascertained and that a comprehensive approach is needed by looking at a series of interactions between different factors and processes that influence chronic somatic symptoms (Vlaeyen et al., 2022). Already in the 1970s, researchers began to shift away

from a solely biomedical perspective to a more holistic approach to understanding chronic somatic symptoms by including a psychological and social perspective to the biomedical model as proposed by George Engel (Engel, 1977). From this, the biopsychosocial model was born and applied to a number of chronic somatic symptoms, including chronic pain and chronic itch, which are thought to be influenced by an amalgamation of biological (e.g., genetics, age), psychological (e.g., expectancies, affect), social (e.g., culture, social interactions), and behavioral (e.g., avoidance) factors that work together to influence both the perception and maintenance of somatic sensations (Gatchel et al., 2007; Melzack, 2001; Verhoeven et al., 2008). This shift in focus to include psychological and social factors has triggered a myriad of research into cognitive-affective and behavioral mechanisms that can be targeted in treatment to complement the biomedical approach. In this regard, two factors have been identified as key mechanisms in the perception and maintenance of chronic somatic symptoms: expectancies (cognitive) and avoidance (behavior).

EXPECTANCIES:

Effects on somatic perception and behavior?

Expectations, or expectancies, can be generally defined as an anticipation of something that will or is about to happen. While the term expectations and expectancies have often been used interchangeably, the term expectancies often encompass the broader concept of expecting and/or predicting, whereas expectations refer to specific or concrete predictions (Janzen et al., 2006).

Expectancies have been shown to shape the perception of somatic sensations. For example, negative expectancies can lead to the aggravation of sensations whereas positive expectancies can lead to alleviation (Evers et al., 2019; Peerdeman et al., 2016; Wolters et al., 2019). These expectancies can be acquired from either instructional learning (i.e., verbal suggestions), experiential learning (e.g. classical conditioning), and/or observational learning (e.g., by observing how others react) (Atlas & Wager, 2012; Blythe et al., 2023; Thomaidou et al., 2023).

There are individual differences in the degree to which expectancies influence somatic perception. It can be partly explained by neural differences (such as increased activity in specific brain regions; Koban et al., 2013; Scott et al., 2007) and trait differences (such as optimism and suggestibility; Kern et al., 2020; Stein et al., 2025), but to date, no single cause that explains these individual differences has been consistently identified (Warner,

2023). Nevertheless, targeting expectancies have been shown to be useful in clinical practice as expectancies can be modified with new information that is gained from interactions with others and daily life experiences (see **Chapter 2** for further details). In addition to influencing somatic perception, expectancies also hold an important function in daily life. More specifically, they help to orient us towards certain actions that may lead to a desirable outcome, or away from behaviors that may lead to an undesirable effect (Roese & Sherman, 2007). One specific form of behavior that expectancies can influence in the context of chronic somatic symptoms is avoidance.

AVOIDANCE:

Role in somatic sensation and expectancies?

Avoidance is a type of action that is performed in anticipation of an unwanted cue as opposed to in reaction to something (the latter would be defined as escape), and can be both behavioral and cognitive (e.g., attentional avoidance). In somatic sensations, avoidance is an evolutionary reaction to protect the body from something that may be damaging. For example, we learn to avoid electric fences to prevent pain from electrocution, or to avoid poison ivy to prevent itchy skin rashes. However, these avoidance behaviors often come at a cost, such as having a limited range of motion when avoiding certain movements or having limited clothing options when avoiding certain types of itch-inducing clothes. Furthermore, too much avoidance can lead to the opposite of the desired effect, where instead of preventing the occurrence of an aversive sensation, it can instead lead to more somatic sensations. Indeed, this is what was theorized in the fear-avoidance model. The fear-avoidance model was first introduced in 1983 in the context of chronic pain (Crombez et al., 2012; Lethem et al., 1983; Vlaeyen et al., 2016), and parts of it has since been applied to chronic itch (Silverberg et al., 2018), and chronic fatigue (Bol et al., 2010). This model posits that when an individual experiences a somatic sensation (e.g., pain), they can interpret this sensation as something that can be experienced from time to time, or as something that is catastrophic. If somatic sensations are interpreted as something that is catastrophic, it can trigger a prolonged avoidance reaction, which instead of preventing the unwanted sensation, may paradoxically lead to worsening. According to this model, a major cause of this paradoxical effect is the restriction in physical activities (meaning that one has less experience with certain somatic sensations) which can increase the risk of somatic sensitivity (Kroska, 2016; Vlaeyen & Linton, 2000). Thus, avoidance no longer has the same protective properties long-term.

Since the initial development of the fear-avoidance model, a multitude of studies have been conducted to pinpoint how the fear-avoidance relationship contributes to the maintenance of chronic somatic symptoms, particularly in the field of pain. A major development in the field of pain is the finding that the fear-avoidance relationship is context dependent, meaning that even if one is fearful of a somatic sensation, they may not necessarily perform avoidance behaviors if there are other goals that motivate a different behavior (Meulders, 2020; Vlaeyen et al., 2016). The role of context illustrates the complexity in the interaction between cognitive-affective and behavioral factors behind chronic somatic symptoms, which still require further evaluation.

SOMATIC SENSATIONS:

Influenced by the interplay between expectancies and avoidance?

As described so far, both expectancies and avoidance play a major role in somatic perception. Expectancy is one of the main drivers of avoidance, and avoidance can aggravate somatic sensations and perception in the long term. However, there are a few gaps in the field that warrant investigation. Firstly, most studies on the relationship between expectancy and avoidance have mainly been done in pain, and very little on other somatic sensations; thus, it is unclear whether certain expectancy-avoidance relationships are sensation specific (e.g., occurs only in pain), or whether they can be generalized across all types of somatic sensations (e.g., occurs in pain, itch, and fatigue). Secondly, from the limited research investigating the relationship between expectancy and avoidance, it is still unclear how these two factors interact with one other across time. Finally, although there are indications that expectancies influence avoidance behavior, there are no studies that investigate the causal relation between the two mechanisms across different types of somatic sensations, and even fewer studies investigating the opposite relation, i.e., the effect of avoidance on expectancies, neither in individuals with chronic somatic symptoms nor in individuals without such symptoms. Therefore, it is important to address these gaps in research as it not only advances the knowledge of understudied mechanisms in different somatic sensations but can also help us identify specific interactions that can be targeted in treatment that may be applicable across different types of chronic somatic symptoms.

THE CURRENT DISSERTATION

This dissertation aims to investigate the relationship between expectancies and avoidance behavior in different somatic sensations. We specifically investigate this relationship on pain, itch, and fatigue as these mechanisms share the same evolutionary role to protect the body and have been shown to share similar transdiagnostic factors that maintain them (discussed further in **Chapter 2**). Different methods were used to investigate this relationship, from theoretical review to experimental studies and ecological momentary assessments, to gain a comprehensive understanding of the expectancy-avoidance relationship within the context of somatic sensations.

In **Chapter 2** we summarize the current state of the art on the relationship between expectancy and avoidance across three chronic somatic symptoms namely: pain, itch, and fatigue. This chapter presents theoretical evidence on the expectancy-avoidance relationship that has been put forth throughout the years and proposes a new integrative model of chronic somatic symptoms taking into account major frameworks across different fields, specifically the predictive coding and active inference perspective.

Chapter 3 takes the first step into directly assessing the influence of expectancies on avoidance behavior in pain. This chapter covers two related studies that investigate whether negative expectancy learning increases pain and pain-avoidance behavior. *Study 1* investigates this relationship using a novel pain avoidance task designed to experimentally mimic the cost-benefit ratio of performing avoidance behavior in daily life, while *Study 2* replicates the design of *Study 1* with improvements to the avoidance task based on results from *Study 1*.

To follow up, we conducted the first experimental study assessing the causal role of expectancies and avoidance in the field of itch in **Chapter 4**. As studies investigating the relation between expectancies and avoidance behavior in itch are scarce, we specifically aimed to evaluate whether negative expectancies led to more costly itch related avoidance behavior. This relationship was investigated using a novel itch-avoidance paradigm in which avoidance was measured using effortful gripping.

To study mechanisms in chronic somatic symptoms, it is important to not only test them, but to also observe the mechanisms in individuals with lived experiences. Thus, in **Chapter 5**, we conducted a study exploring the relationship between avoidance, expectancies, pain, and other psychological mechanisms that constitute cognitive-affective and behavioral factors in individuals with chronic low back pain. This study measured individuals' pain and

psychological mechanisms throughout the day across two weeks and utilized the network approach to compute and visualize the connections between pain and related cognitive-affective and behavioral factors.

Finally, **Chapter 6** summarizes the findings of this dissertation and discusses the implications of the expectancy-avoidance relationship in somatic sensations. This chapter also addresses the limitations of this dissertation and explores directions for future research.

REFERENCES

Atlas, L. Y., & Wager, T. D. (2012). How expectations shape pain. *Neuroscience Letters*, 9. https://doi.org/doi:10.1016/j.neulet.2012.03.039

Blythe, J. S., Thomaidou, M. A., Peerdeman, K. J., van Laarhoven, A. I. M., van Schothorst, M. M. E., Veldhuijzen, D. S., & Evers, A. W. M. (2023). Placebo effects on cutaneous pain and itch: A systematic review and meta-analysis of experimental results and methodology. *PAIN*, *164*(6), 1181. https://doi.org/10.1097/j.pain.0000000000002820

Bol, Y., Duits, A. A., Lousberg, R., Hupperts, R. M. M., Lacroix, M. H. P., Verhey, F. R. J., & Vlaeyen, J. W. S. (2010). Fatigue and physical disability in patients with multiple sclerosis: A structural equation modeling approach. *Journal of Behavioral Medicine*, *33*(5), 355–363. https://doi.org/10.1007/s10865-010-9266-8

Boullosa, D. A., & Nakamura, F. Y. (2013). The evolutionary significance of fatigue. *Frontiers in Physiology*, *4*, 309. https://doi.org/10.3389/fphys.2013.00309

Cohen, S. P., Vase, L., & Hooten, W. M. (2021). Chronic pain: An update on burden, best practices, and new advances. *The Lancet*, *397*(10289), 2082–2097. https://doi.org/10.1016/S0140-6736(21)00393-7

Cole, E., Yeung, H., & Chen, S. (2021). The quality of life impact of chronic itch compared to pain. In G. Yosipovitch, H. H. Andersen, & L. Arendt-Nielsen (Eds.), *Itch and Pain: Similarities, Interactions, and Differences* (pp. 10–21). Wolters Kluwer.

Crombez, G., Eccleston, C., Van Damme, S., Vlaeyen, J. W. S., & Karoly, P. (2012). Fear-avoidance model of chronic pain: The next generation. *The Clinical Journal of Pain*, *28*(6), 475–483. https://doi.org/10.1097/AJP.0b013e3182385392

Eccles, J. A., & Davies, K. A. (2021). The challenges of chronic pain and fatigue. *Clinical Medicine*, *21*(1), 19. https://doi.org/10.7861/clinmed.2020-1009

Engel, G. L. (1977). The Need for a New Medical Model: A Challenge for Biomedicine. *Science*, *196*(4286), 129–136. https://doi.org/10.1126/science.847460

Evers, A. W. M., Peerdeman, K. J., & Laarhoven, A. I. M. (2019). What is new in the psychology of chronic itch? *Experimental Dermatology*, *28*(12), 6. https://doi.org/10.1111/exd.13992

Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychological Bulletin*, *133*(4), 581–624. https://doi.org/10.1037/0033-2909.133.4.581

Gerbershagen, H. U., Lindena, G., Korb, J., & Kramer, S. (2002). Health-related quality of life in patients with chronic pain. *Schmerz (Berlin, Germany)*, *16*(4), 271–284. https://doi.org/10.1007/s00482-002-0164-z

Janzen, J. A., Silvius, J., Jacobs, S., Slaughter, S., Dalziel, W., & Drummond, N. (2006). What is a health expectation? Developing a pragmatic conceptual model from psychological theory. *Health Expectations*, *9*(1), 37–48. https://doi.org/10.1111/j.1369-7625.2006.00363.x

Kern, A., Kramm, C., Witt, C. M., & Barth, J. (2020). The influence of personality traits on the placebo/nocebo response: A systematic review. *Journal of Psychosomatic Research*, *128*, 109866. https://doi.org/10.1016/j.jpsychores.2019.109866

Koban, L., Ruzic, L., & Wager, T. D. (2013). Chapter 10—Brain Predictors of Individual Differences in Placebo Responding. In L. Colloca, M. A. Flaten,

& K. Meissner (Eds.), *Placebo and Pain* (pp. 89–102). Academic Press. https://doi.org/10.1016/B978-0-12-397928-5.00010-6

Kroska, E. B. (2016). A meta-analysis of fear-avoidance and pain intensity: The paradox of chronic pain. *Scandinavian Journal of Pain*, *13*(1), 43–58. https://doi.org/10.1016/j.sjpain.2016.06.011

Lenaert, B., Boddez, Y., Vlaeyen, J. W., & van Heugten, C. M. (2018). Learning to feel tired: A learning trajectory towards chronic fatigue. *Behaviour Research and Therapy*, *100*, 54–66. https://doi.org/10.1016/j.brat.2017.11.004

Lethem, J., Slade, P., Troup, J. D. G., & Bentley, G. (1983). Outline of a fear-avoidance model of exaggerated pain perception.1. *Behaviour Research and Therapy*, *21*, 401–408. https://doi.org/10.1016/0005-7967(83)90009-8

Liu, T., & Ji, R.-R. (2013). New insights into the mechanisms of itch: Are pain and itch controlled by distinct mechanisms? *Pflugers Archiv : European Journal of Physiology*, *465*(12), 10.1007/s00424. https://doi.org/10.1007/s00424-013-1284-2

Melzack, R. (2001). Pain and the Neuromatrix in the Brain. *Journal of Dental Education*, *65*(12), 1378–1382. https://doi.org/10.1002/j.0022-0337.2001.65.12.tb03497.x

Meulders, A. (2020). Fear in the context of pain: Lessons learned from 100 years of fear conditioning research. *Behaviour Research and Therapy*, *131*, 103635. https://doi.org/10.1016/j.brat.2020.103635

Noakes, T. D. (2012). Fatigue is a Brain-Derived Emotion that Regulates the Exercise Behavior to Ensure the Protection of Whole Body Homeostasis. *Frontiers in Physiology*, *3*. https://doi.org/10.3389/fphys.2012.00082

Peerdeman, K. J., Laarhoven, A. I. M. van, Peters, M. L., & Evers, A. W. M. (2016). An Integrative Review of the Influence of Expectancies on Pain. *Frontiers in Psychology*, *7*. https://doi.org/10.3389/fpsyg.2016.01270

Petersen, G. L., Finnerup, N. B., Colloca, L., Amanzio, M., Price, D. D., Jensen, T. S., & Vase, L. (2014). The magnitude of nocebo effects in pain: A meta-analysis. *Pain*, *155*(8), 1426–1434. https://doi.org/10.1016/j.pain.2014.04.016

Phillips, C. J. (2009). The Cost and Burden of Chronic Pain. *Reviews in Pain*, *3*(1), 2. https://doi.org/10.1177/204946370900300102

Racine, M., Hudson, M., Baron, M., Nielson, W. R., Pope, J., Markland, J., Robinson, D., Jones, N., Khalidi, N., Docherty, P., Kaminska, E., Masseto, A., Sutton, E., Mathieu, J.-P., Ligier, S., Grodzicky, T., Thorne, C., Gyger, G., Smith, D., … Larché, M. (2016). The Impact of Pain and Itch on Functioning and Health-Related Quality of Life in Systemic Sclerosis: An Exploratory Study. *Journal of Pain and Symptom Management*, *52*(1), 43–53. https://doi.org/10.1016/j.jpainsymman.2015.12.314

Raja, S. N., Carr, D. B., Cohen, M., Finnerup, N. B., Flor, H., Gibson, S., Keefe, F. J., Mogil, J. S., Ringkamp, M., Sluka, K. A., Song, X.-J., Stevens, B., Sullivan, M. D., Tutelman, P. R., Ushida, T., & Vader, K. (2020). The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. *PAIN*, *161*(9), 1976. https://doi.org/10.1097/j.pain.0000000000001939

Rasmussen, S., Jensen, C. T., Rosendal, M., Vægter, H. B., Søndergaard, J., & Jarbøl, D. E. (2020). Multiple physical symptoms and individual characteristics – A cross-sectional study of the general population. *Journal of Psychosomatic Research*, *131*,

109941. https://doi.org/10.1016/j.jpsychores.2020.109941

Roese, N. J., & Sherman, J. W. (2007). Expectancy. In *Social psychology: Handbook of basic principles, 2nd ed* (pp. 91–115). The Guilford Press.

Ross, S. E. (2011). Pain and itch: Insights into the neural circuits of aversive somatosensation in health and disease. *Current Opinion in Neurobiology*, *21*(6), 880–887. https://doi.org/10.1016/j.conb.2011.10.012

Scott, D. J., Stohler, C. S., Egnatuk, C. M., Wang, H., Koeppe, R. A., & Zubieta, J.-K. (2007). Individual Differences in Reward Responding Explain Placebo-Induced Expectations and Effects. *Neuron*, *55*(2), 325–336. https://doi.org/10.1016/j.neuron.2007.06.028

Silverberg, J. I., Kantor, R. W., Dalal, P., Hickey, C., Shaunfield, S., Kaiser, K., Lai, J.-S., & Cella, D. (2018). A comprehensive conceptual model of the experience of chronic itch in adults. *American Journal of Clinical Dermatology*, *19*(5), 759–769. https://doi.org/10.1007/s40257-018-0381-6

Stander, S., Weisshaar, E., Mettang, T., Szepietowski, J. C., Carstens, E., Ikoma, A., Bergasa, N. V., Gieler, U., Misery, L., & Wallengren, J. (2007). Clinical classification of itch: A position paper of the International Forum for the Study of Itch. *Acta Dermato-Venereologica*, *87*(4), 291–294. https://doi.org/10.2340/00015555-0305

Stein, M. V., Heller, M., Chapman, S., Rubin, G. J., & Terhune, D. B. (2025). Trait responsiveness to verbal suggestions predicts nocebo responding: A meta-analysis. *British Journal of Health Psychology*, *30*(1), e12774. https://doi.org/10.1111/bjhp.12774

Thomaidou, M. A., Blythe, J. S., Peerdeman, K. J., van Laarhoven, A. I. M., Van Schothorst, M. M. E., Veldhuijzen, D. S., & Evers, A. W. M. (2023). Learned Nocebo Effects on Cutaneous Sensations of Pain and Itch: A Systematic Review and Meta-analysis of Experimental Behavioral Studies on Healthy Humans. *Psychosomatic Medicine*, *85*(4), 308–321. https://doi.org/10.1097/PSY.0000000000001194

Treede, R.-D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., Cohen, M., Evers, S., Finnerup, N. B., First, M. B., Giamberardino, M. A., Kaasa, S., Korwisi, B., Kosek, E., Lavand'homme, P., Nicholas, M., Perrot, S., Scholz, J., Schug, S., … Wang, S.-J. (2019). Chronic pain as a symptom or a disease: The IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *PAIN*, *160*(1), 19. https://doi.org/10.1097/j.pain.0000000000001384

Van Heck, G. L., & de Vries, J. (2002). Quality of life of patients with chronic fatigue syndrome. *Journal of Chronic Fatigue Syndrome*, *10*(1), 17–35. https://doi.org/10.1300/J092v10n01_03

Verhoeven, E. W. M., de Klerk, S., Kraaimaat, F. W., van de Kerkhof, P. C. M., de Jong, E. M. G. J., & Evers, A. W. M. (2008). Biopsychosocial mechanisms of chronic itch in patients with skin diseases: A review. *Acta Dermato-Venereologica*, *88*(3), 211–218. https://doi.org/10.2340/00015555-0452

Vesterling, C., Schütz-Wilke, J., Bäker, N., Bolz, T., Eilts, J., Koglin, U., Rademacher, A., & Goagoses, N. (2023). Epidemiology of Somatoform Symptoms and Disorders in Childhood and Adolescence: A Systematic Review and Meta-Analysis. *Health & Social Care in the Community*, *2023*(1), 6242678. https://doi.org/10.1155/2023/6242678

Vlaeyen, J. W. S., Crombez, G., & Linton, S. J. (2016). The fear-avoidance model of pain. *Pain*, *157*(8), 1588–1589. https://doi.org/10.1097/j.pain.0000000000000574

Vlaeyen, J. W. S., Haslbeck, J. M. B., Sjouwerman, R., & Peters, M. L. (2022). Towards a dynamic account of chronic pain. *PAIN*, *163*(9), e1038. https://doi.org/10.1097/j.pain.0000000000002706

Vlaeyen, J. W. S., & Linton, S. J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. *Pain*, *85*(3), 317–332. https://doi.org/10.1016/S0304-3959(99)00242-0

Wall, P. D. (1979). On the relation of injury to pain the John J. Bonica Lecture. *PAIN*, *6*(3), 253. https://doi.org/10.1016/0304-3959(79)90047-2

Walters, E. T., & Williams, A. C. de C. (2019). Evolution of mechanisms and behaviour important for pain. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *374*(1785), 20190275. https://doi.org/10.1098/rstb.2019.0275

Warner, J. O. (2023). Placebo/nocebo responses in clinical trials and practice. *Current Allergy & Clinical Immunology*, *36*(4), 2–6. https://doi.org/10.10520/ejc-caci-v36-n4-a6

Wolters, F., Peerdeman, K. J., & Evers, A. W. M. (2019). Placebo and nocebo effects across symptoms: From pain to fatigue, dyspnea, nausea, and itch. *Frontiers in Psychiatry*, *10*, 470. https://doi.org/10.3389/fpsyt.2019.00470