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

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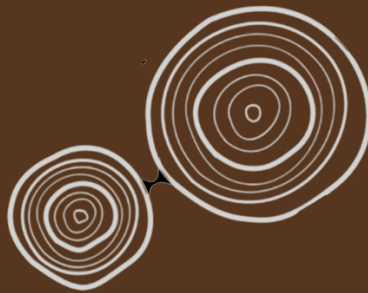
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# CHAPTER 2

## Expectancies and Avoidance: Towards an Integrated Model of Chronic Somatic Symptoms



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## 1. INTRODUCTION

Somatic symptoms like pain, itch, and fatigue, can negatively affect daily functioning. In the acute phase, these somatic symptoms are adaptive as they push the body to protect itself from potential bodily threat. However, when these symptoms turn chronic, they may instead cause disability. Pain, itch, and fatigue have been shown to share mechanisms that maintain them towards chronicity, and they commonly occur in various medical conditions. For example, pain and fatigue are common co-occurring symptoms in patients with multiple sclerosis, cancer, chronic low back pain, fibromyalgia, and functional neurological disorders (e.g., Eccles and Davies, 2021; Maggio et al., 2020; Mense and Schiltenswolf, 2010; Petersen et al., 2020) and symptoms of itch, pain, and fatigue are often reported in patients with chronic skin diseases and other chronic conditions, such as some forms of cancer or kidney disease (e.g., Verhoeven et al., 2007). Additionally, each of these symptoms have a high prevalence rate (Dahlhamer et al., 2018; Lim et al., 2020; Weisshaar, 2016) and share the same evolutionary function; to protect the body from disease and harm (Boullosa and Nakamura, 2013; Cevikbas and Lerner, 2020; Walters and Williams, 2019). Furthermore, chronic pain, itch, and fatigue cause similar burden to those that experience them. These chronic symptoms can also limit productivity and interfere with daily activities which have been shown to lower quality of life (Cole et al., 2021; Gerbershagen et al., 2002; Van Heck & de Vries, 2002). Moreover, the stigma that may be associated with these symptoms could also contribute to low quality of life (Froehlich et al., 2022; Perugino et al., 2022; Warlich et al., 2015).

Due to the large impact of chronic somatic symptoms, researchers have tried to identify the underlying mechanisms and processes that maintain them. One way to better understand chronic somatic symptoms is by using a transdiagnostic approach in which shared mechanisms are evaluated (e.g., Harvey et al., 2004; Linton, 2013). Specifically, expectancy and avoidance learning are two transdiagnostic mechanisms that have been thought to play a key role in chronic somatic conditions (Evers et al., 2019; Lenaert et al., 2018; Peerdeman et al., 2016; Silverberg et al., 2018; Vlaeyen and Crombez, 2020). However, despite potential indications that expectancies and avoidance mechanisms are intertwined, how expectancies drive avoidance and vice versa, and how both contribute to the maintenance of chronic somatic symptoms remains understudied. Thus, in this current article, we propose an integrated theoretical model on the interplay between expectancy and avoidance behavior across symptoms of pain, itch, and fatigue. Our goal is to explain how these mechanisms interact in symptom perception using the basic principles of the predictive coding and active

inference perspective. For more detailed and technical explanations of these frameworks, we refer to the following papers: (Friston, 2010; Friston et al., 2017; Hohwy, 2017; Smith et al., 2022). Finally, we discuss the clinical implications and future directions in this field.

## 2. EXPECTANCIES IN SOMATIC SYMPTOMS

Expectancy plays a large role in the processing of somatic symptoms. In fact, various scholars have argued that expectancy is a core mechanism in persistent somatic symptoms including chronic fatigue syndrome and fibromyalgia (Van den Bergh et al., 2017). Based on different theoretical frameworks, there are several kinds of expectancies that can influence both symptom perception and treatment outcomes (Evers et al., 2019; Peerdeman et al., 2016; Rief et al., 2015; Van den Bergh et al., 2017). For example, self-efficacy expectancies, or expectancies relating to one's own ability, have been proposed based on the self-efficacy theory. Additionally, based on the response expectancy theory, outcome expectancies (e.g., expecting to feel a somatic symptom) can be divided into two parts, namely: response expectancies (defined as a type of expectancy involving one's own reaction towards something) and stimulus expectancies (defined as a type of expectancy relating to an external object or substance) (Kirsch, 2018, 1997, 1985). These expectancies can be formed through different learning mechanisms and studies have shown that a combination of instructional and associative learning produce the strongest expectancy effects (Blythe et al., 2023, 2019; Thomaidou et al., 2023).

Research on expectancies has largely been done on outcome expectancies in the context of placebo and nocebo effects. In the field of placebo effects, an ample number of studies have shown that positive expectancies alone, like expecting to experience less symptoms, have the potential to reduce somatic symptoms, (e.g., Bottoms et al., 2014; Broelz et al., 2018; Meissner et al., 2011; van Laarhoven et al., 2015; Vase & Petersen, 2013). On the other hand, when expectancies are negative, like expecting itch to worsen from taking a hot shower, the expectation of itch itself has the potential to lead to symptom induction or worsening (i.e., a nocebo effect), especially when the individual is fearful of the somatic symptom (e.g., Aslaksen and Lyby, 2015; Blasini et al., 2017; Weng et al., 2022; Wolters et al., 2019). Most studies on the role of expectancies have been conducted in the context of pain, and only recently has there been a growing body of literature investigating the effects of expectancies on itch and fatigue (Blythe et al., 2019; Lenaert et al., 2018; Weng et al., 2022; Wolters et al., 2019).

### 3. AVOIDANCE IN SOMATIC SYMPTOMS

Safety behaviors, in particular avoidance, can prevent an individual from experiencing pain, itch, and/or fatigue. One of the theoretical models that explains the shift from acute to chronic somatic symptoms is the fear-avoidance model (FAM) which was developed for chronic pain (Crombez et al., 2012; Vlaeyen & Linton, 2000, 2012), but has now been applied to both fatigue (Bol et al., 2010) and itch (Silverberg et al., 2018). The FAM posits that the experience of a somatic symptom can elicit fear, which in turn triggers an avoidance reaction. Avoidance entails that a behavior is altered in anticipation of a negative stimulus as opposed to in response to the actual negative stimulus. These avoidance behaviors can take shape in various ways across symptoms, such as abstaining from movement and activities (Crombez et al., 2012; Heins et al., 2013; Kroska, 2016), avoidance of wearing wooly clothing (Silverberg et al., 2018), and even withdrawing from social events (Philips, 1987; Ruscheweyh et al., 2019). These avoidance behaviors often begin as an adaptive mechanism to prevent symptom worsening and to provide a sense of control over symptom occurrence (Lenaert et al., 2018). However, long-term avoidance behavior in the absence of threat can lead to adverse effects and increase the risk of disability especially when it generalizes to new stimuli (Crombez et al., 2012; Meulders, 2019; Vlaeyen and Linton, 2012). Since its conception (Lethem et al., 1983; Vlaeyen et al., 1995), the FAM has kindled numerous studies across different contexts on how (dysfunctional) avoidance is learned (e.g., Jepma et al., 2022; Meulders, 2019; Volders et al., 2015), how it influences different chronic conditions (e.g., (Bonnert et al., 2018; Hedman-Lagerlöf et al., 2019; Knoop et al., 2010; Lenaert et al., 2018; Picon et al., 2021; Snell et al., 2023), and how it can be reduced in clinical treatment (e.g., Meulders et al., 2015; Nicholas et al., 2014; Yang et al., 2022). Therefore, a deeper understanding of the factors influencing both adaptive and dysfunctional avoidance behavior may help to reduce the chronification and other consequences of chronic somatic symptoms.

### 4. EVOLUTION OF EXPECTANCY AND AVOIDANCE THEORETICAL MODELS

Over the years, various theories and models have been proposed that assume an association between expectancies and avoidance. From animal studies to psychopathology, avoidance has been considered as a product of associative and instrumental learning. This idea dates as far back to the early 1900s when Edward Tolman introduced a cognitive component to avoidance behavior. Based on animal models, Tolman argued that both animals and humans

can build a cognitive map of their environment that can be used to learn which stimuli should be avoided (see e.g., Tolman, 1948). This cognitive map was an early indication of how expectancies can be acquired to prevent unwanted stimuli.

Throughout the course of time, this cognitive aspect of avoidance behavior has been expanded and applied to human behavior. In the early 1950's the two-factor theory was proposed by Orval Hobart Mowrer in which avoidance behavior was thought to be driven by fear acquired from both Pavlovian and instrumental learning (Mowrer, 1951). This theory was highly influential for the development of behavioral therapies which became the basis of many clinical treatments that are being used today such as cognitive behavioral therapy. Subsequently, Seligman and Johnston (1973) proposed that in addition to the acquired fear, individuals also perform avoidance behaviors because they expect that by performing an avoidance behavior, an aversive stimulus will not be received. This idea was further extrapolated by other researchers, adding more complexity of the cognitive processes behind avoidance. For example, Rachman & Arntz (1991) proposed that the experience of pain is influenced by people's prediction (i.e., expectancy) of the intensity of pain, and that these predictions can change depending on whether there is a match between their past expectancies of pain and the actual pain that is experienced. Relatedly, Marks and de Silva (1994) introduced the match/mismatch model of fear and described the effects of over- and underpredictions of fear on avoidance behavior in anxiety-related conditions (e.g., snakes and spider phobia, panic disorder) as well as pain. Later, the cognitive model of avoidance behavior by Seligman and Johnson (1973) was expanded by Lovibond (2006) to include situational factors such as environmental cues or subjective interpretations of a situation in both Pavlovian (classical) and instrumental learning of avoidance. In this model, they argued that avoidance behavior can be acquired by gathering information about the relationship between a warning signal and an aversive outcome, and that one can learn to prevent an aversive outcome by performing an avoidance behavior, proposing that expectancy is the main driver in this learning process of avoidance behavior.

All these models assume a relationship in which different conceptualizations of expectancies can influence avoidance behavior over time and contribute to symptom worsening. However, despite indications of a link between expectancies and avoidance, this topic is still understudied in somatic symptoms like pain, itch, fatigue. Therefore, we build on past theoretical learning models and connect them to more recent theories with a central expectation component, specifically predictive coding and Bayesian approaches, to gain a better understanding of the inner workings behind chronic somatic symptoms.

## 5. THE EXPECTANCY-AVOIDANCE MODEL OF CHRONIC SOMATIC SYMPTOMS

In recent years, several approaches have been put forth that conceptualize the maintenance of somatic symptoms (e.g., Kube et al., 2020; Van den Bergh et al., 2017) like pain (e.g., Büchel et al., 2014; Eckert et al., 2022; Lersch et al., 2023; Milde et al., 2024; Tabor and Burr, 2019) and dyspnea (e.g., Marlow et al., 2019; Peiffer, 2023; Pezzulo et al., 2019) using Bayesian inference and the predictive coding perspective. Bayesian inference is a statistical method that can be applied to human behavior and cognition to explain how we make sense of the world using a series of predictions (i.e., expectations) that are made based on the information that we receive (Griffiths et al., 2008). These predictions not only include conscious verbalizable expectations, but also implicit expectations that can be embodied through autonomic responses and activation of the hypothalamic-pituitary-adrenal axis (Kiverstein et al., 2022). Relatedly, a type of Bayesian inference called the predictive coding perspective tries to explain how our perception is influenced by constant predictive processes to generate accurate models of the world (Friston, 2010). More specifically, different processes can influence the world that we perceive (or in computational terms called *posteriors*), which is constructed based on a combination of existing knowledge (called prior beliefs or *priors*) and incoming information from the external world (called *likelihood*) (Griffiths et al., 2008). This can be translated to somatic symptoms where expectations about pain, itch, and fatigue serve as the priors, sensory input such as heat or tactile stimulation serve as the likelihood, and the perceived sensation serves as the posterior model. Thus, the synthesis of both top-down (i.e., expectations) and bottom-up processes (sensory input) constitutes how intensely we perceive somatic sensations (Maisto et al., 2021).

However, our expectations of a somatic sensation and actual sensory input can differ. When this happens, prediction errors occur (Hohwy, 2017). According to the free energy principle, we are inherently driven to reduce prediction errors in order to maintain a state of equilibrium (Friston, 2010; Friston et al., 2017, 2016). These prediction errors can be minimized by either adjusting existing expectations based on incoming sensory input and generating new posteriors, or through active inference by gathering information to fit the prior (Van den Bergh et al., 2017). The (partly unconscious) strategy used to minimize prediction error is based on the relative precisions of the priors and the prediction error. Because priors and prediction errors can be thought of as probability distributions of neural activity, precisions can be defined as the inverse variance associated with each probability distribution representing the level of certainty/confidence (or reliability) that a neural

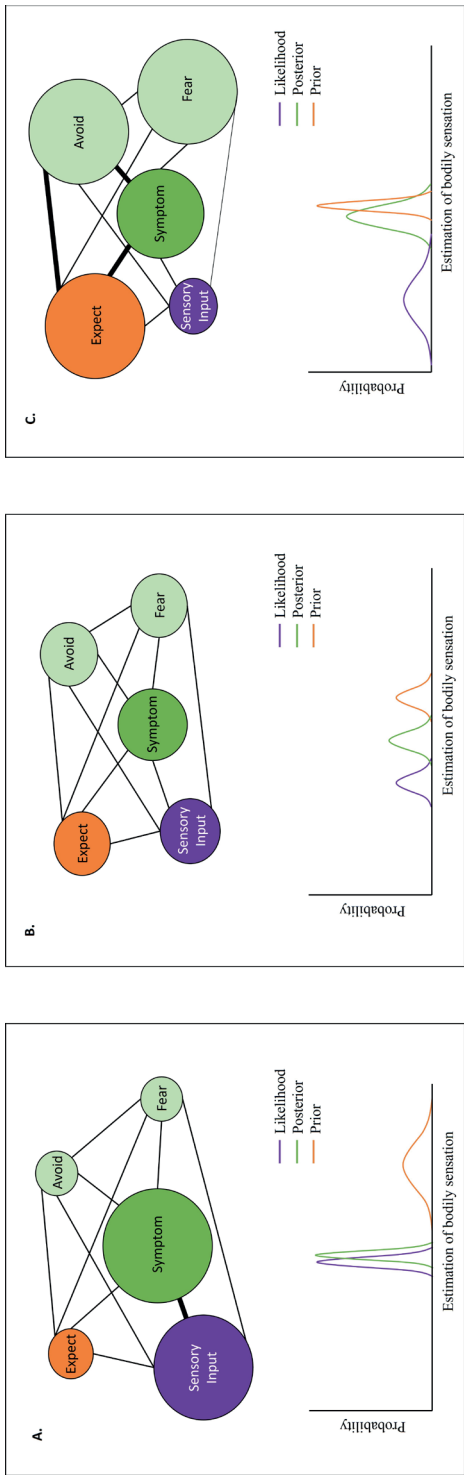
pattern is associated with a certain input. Precisions act as weighing factors in the balance to minimize prediction errors by attributing more weight to either the prior or to the prediction errors (Feldman and Friston, 2010; Friston, 2010; Hohwy, 2017). Fig. 1a-c shows how perception can change based on different precision levels. For example, the perception of somatic symptoms is expected to be equally influenced by prior expectations and incoming sensory input when both of these sources of information are similarly precise (Fig. 1b). This is the case when we feel fatigue after working out. How strongly we feel fatigue is influenced by both the expectation that we will feel tired after lifting weights (precise expectancies) and by lifting heavy weights (precise sensory input). However, our perception of symptoms could also be based relatively more on the incoming sensory input, rather than our expectations (Fig. 1a). For example, imagine trying a new soothing emollient (high precise sensory input) that unexpectedly (low precise expectancies) triggers an allergic reaction for the first time. How intensely we perceive the allergy would be based on the sensory input coming from the emollient as opposed to our expectations as more weight is put on the precise sensory input than expectations. In contrast, if individuals have highly precise expectations (Fig. 1c), individuals will rely more on their expectations rather than uncertain incoming sensory input. These highly precise expectations could generate a misperception of symptoms as the highly precise expectations might not reflect the sensory input (Maisto et al., 2021; Milde et al., 2024). This could explain how somatic symptoms can be perceived after encountering harmless stimuli (Adamczyk et al., 2019) and also how placebo instructions can lead to pain reduction (Milde et al., 2024).

Taking this together, we propose an expectancy-avoidance model of chronic somatic symptoms (see Fig. 1a-c). In this model, we view the relationship between expectancies and avoidance behavior through an active inference perspective in which individuals with chronic pain, itch, and fatigue try to minimize prediction errors through action selection. In choosing which action to select, the individual has to weigh the options between reward-seeking behaviors (i.e., actions that lead to the most desired outcome) and information-seeking behaviors (i.e., actions that help reduce uncertainty in current states) (Maisto et al., 2021). The action selected is determined based on the behavior that will lead to the least uncertainty and the most rewarding outcome (Friston et al., 2016; Smith et al., 2022). Therefore, reward-seeking behaviors are often prioritized in case of high certainty in predicted states (e.g., “I am sure that my leg will not itch if I apply this cream”), whereas information-seeking behaviors are often prioritized in ambiguous situations (e.g., increasing attention towards a tingling sensation that may indicate itch). Here, we propose that highly precise

expectancies about pain, itch, and fatigue could trigger avoidance behavior in situations that previously led to somatic symptoms, therefore prioritizing the most rewarding outcome (i.e., feeling free of somatic symptoms), as opposed to gathering information to determine whether one is experiencing somatic symptoms in the first place in the short term. This protective strategy has been shown to be associated with perceived threat and a dispositional negativity trait often found in different psychopathological conditions like anxiety disorders (Van den Bergh et al., 2021). Moreover, these highly precise expectations influence fearful cognitions and beliefs (Pezzulo, 2014), which are strongly related to avoidance behavior. Some evidence of the expectancy-avoidance relationship can already be seen in healthy participants in which expectations of pain were shown to be associated with more avoidance-related movements in the short term (Janssens et al., 2019). The expectancy-avoidance model highlights not only the central role of expectancies, but also the importance of limiting avoidance behavior by weighing the precision level of different sources of information.

As mentioned previously, active inference can reduce prediction errors resulting from highly precise priors and low precise sensory input. Here, two types of priors can motivate behavior: prior beliefs and prior preferences or goals (Maisto et al., 2021). In case of chronic somatic symptoms, prior beliefs often take shape as expectations related to the increase of somatic symptoms, while prior preferences or goals can take shape as the desire to be free of somatic symptoms. In turn, these highly precise priors generate behaviors that are expected to lead to less somatic symptoms. If these expectations are coupled with noisy sensory input, then the behavior that is performed is driven by the most reliable information, which in this case is the highly precise expectations. Take for example a person that is deciding whether or not to rest. A healthy individual would first need to infer whether they are feeling fatigued, before deciding to rest. They can do so by drawing more attention to any sensory input that might indicate fatigue. However, in individuals with chronic fatigue syndrome with strong expectations that they will feel fatigued, the best action to take to prevent further fatigue is to rest (thereby leading to the most rewarding outcome) without first gathering information on the level of fatigue.

**Figure 1.** Proposed expectancy-avoidance model of somatic symptoms.



Panel A, B, C reflects the pathways of the expectancy-avoidance-symptom relationship based on different precision levels. Thicker lines indicate stronger relationships, and larger node sizes indicate degree of precision of that factor. The color of nodes corresponds to the color of the probability distributions below (i.e., orange indicates priors, purple indicates likelihoods, and green reflects posteriors). Panel A depicts the interaction between expectancy and avoidance with highly precise sensory input and a less precise prior. Here, symptom perception and behavior are highly influenced by the likelihood (e.g., sensory input), and priors are more diffused as the individual does not have any strong expectations, for example, experiencing itch after encountering poison ivy, as they expect to feel itch upon touching it. In this instance, expectancies are the main driver of avoidance. Panel B depicts the expectancy-avoidance-symptom connection when priors and likelihood have similar precision. In this case, the posterior is generated close to both the priors and likelihood. This occurs, for instance, when someone expects to feel pain during a needle prick, and experiences pain during a needle prick, like in the case of experiencing new pain treatment involving injections for the first time. Panel C depicts the effect of a highly precise prior on the expectancy-avoidance-symptom relationship. It is proposed that this is the model that applies to many chronic somatic conditions. Here, highly precise priors, such as expecting fatigue could lead to symptom misperception (experiencing fatigue with minimal activity) as it is the most salient information that the individual receives. Thus, the context (e.g., feeling pain/itch/fatigue) has been established. This discrepancy between precise priors and diffused sensory input then initiates fear and avoidance behaviors, to prevent somatic symptoms and match the highly precise priors even in the absence of threatening stimuli.

While changing behavior in anticipation of threatening stimuli has an adaptive component (Morrison, 2013), long-term avoidance can become dysfunctional as it prevents the individual from receiving evidence that disconfirm their expectancies. As time goes on, the precision of the expectancies increases while the precision of incoming sensory input decreases (Ainley et al., 2016). This process can be described as a stagnated error-reduction process in which prediction errors persist because highly precise expectancies are maintained without being corrected by sensory evidence (Maisto et al., 2021; Van den Bergh et al., 2021). This model could explain why it takes multiple trials of disconfirming evidence to change overpredictions (Rachman & Arntz, 1991) as the rate of learning is lower with more precise priors (Hohwy, 2017). If these highly precise, but incorrect negative expectations are maintained, it could lead to higher priority given towards information that confirms that one is experiencing a somatic sensation. Thereby, an individual could be feeling more pain, itch, or fatigue, even with minimal sensory input. Consequently, if intense somatic sensations are perceived, fear and avoidance could generalize to non-threatening stimuli. More avoidance, then maintains fear, negative expectancy, and the perception of symptom worsening even when it may not necessarily be true, thus continuing the (dysfunctional) behavior of avoidance. This illustrates how perception can influence behaviors, and how behaviors can shape perception via expectancies.

Relatedly, different processes can affect the interaction between expectancies and avoidance behaviors. Firstly, interoceptive processes, or the ability to sense internal bodily signals, may affect the processing of incoming sensory information (Barrett and Simmons, 2015), thus influencing the precision of the likelihood. As the accuracy of interoception is often hampered in individuals with chronic pain (Di Lernia et al., 2016) and other chronic conditions (Jungilligens et al., 2022; Locatelli et al., 2023), these individuals may have difficulty learning that a non-painful stimulus such as light pressure is not painful due to the heavy reliance on priors, making it difficult to increase the precision of sensory input (Eckert et al., 2022). Secondly, motivational processes can also influence expectations and the degree of avoidance. Studies have shown how, in pain, people perform avoidance behaviors less if they are given a reward for performing a different (pain-related) behavior (Claes et al., 2015, 2014; Van Damme et al., 2012). Therefore, our (unconscious) decision to avoid is not only influenced by the degree of probability that the expectation will occur (Warren et al., 1989) but also by our goals and motivation (Claes et al., 2015, 2014; Pittig et al., 2020; Van Damme et al., 2012). Expectancies, somatic symptoms, and avoidance then creates an ever-changing dynamic relationship that contributes to chronic pain, itch, and fatigue.

## 6. CHALLENGES, FUTURE DIRECTIONS, AND CLINICAL IMPLICATIONS

So far, we have reviewed the current literature on the relationship between expectancy and avoidance in somatic symptoms such as pain, itch, and fatigue. Although there is theoretical evidence pointing towards the influence of expectancy on avoidance behavior as transdiagnostic mechanisms in somatic symptoms, questions and challenges remain for future studies.

One of the challenges is determining how expectancies maintain avoidance behavior. One way to address this challenge may be to gather more empirical evidence on the expectancy-avoidance-symptom relationship in itch and fatigue, as evidence has mostly been gathered from the field of pain. Furthermore, it is still unclear, how this relationship affect other types of somatic symptoms and other brain-mind-body interface disorders (e.g., disorder of the brain gut interaction), though it should be noted that there is a growing number of studies demonstrating the expectancy-avoidance relationship in chronic dyspnea (Marlow et al., 2019; Peiffer, 2023). Therefore, gathering more empirical evidence on the expectancy-avoidance-symptom relationship across different bodily symptoms can help strengthen the applicability of the proposed model in different somatic symptoms.

Additionally, the role of related psychological constructs in the expectancy-avoidance model may need to be considered. For example, negative expectations can manifest as fear and catastrophizing which plays an important role in the development of avoidance behavior (e.g., Carriere et al., 2015; de Jong & Daniels, 2020; Lovibond, 2006; Meulders, 2019; Peerdeman et al., 2016; Vlaeyen et al., 2016), and negative affect, and psychological distress have also been shown to increase somatic symptoms (Oka, 2013; Sanders and Akiyama, 2018; Woo, 2010), while self-identity have been shown to influence daily functioning in chronic pain (Reed et al., 2022; Yu et al., 2015). Yet, we do not know whether these psychological factors precede or predict expectancy and avoidance, whether they mediate or moderate the relationship between expectancy and avoidance, or whether they are a product of expectancy and avoidance. Thus, it is not yet clear, where exactly these related factors fit in the model. Nevertheless, these factors certainly play an important role in the formation as well as the precision of specific priors. One approach to investigate the mechanisms influencing the maintenance of somatic symptoms is through an interconnected network. In the field of psychopathology, it has been proposed to consider the entire system of potential factors that maintains a disorder (Roefs et al., 2022). Researchers have already proposed a

network model for chronic pain to conceptualize how different psychological constructs interact with each other leading to chronic pain (see Thompson et al., 2019; Vlaeyen et al., 2022). Utilizing the network approach using experimental and observational data may give us insight on where, for instance, fear and other affective responses, such as psychological distress, fit in the expectancy-avoidance model and how different competing goals may influence avoidance behavior.

Another related challenge is determining the best approach to capture expectancies and avoidance. In terms of expectancies, clinical trials often measure expectations using self-report questionnaires once at baseline, and often only measure one type of expectancies, for example, outcome expectancies (e.g., how certain actions will affect symptoms), or self-efficacy expectancies (e.g., how well can one perform an activity, despite their symptoms). However, this only gives us partial information on the influence of expectancies on symptom worsening. Future studies and clinical trials could consider measuring various aspects of behavioral and symptom related expectancies multiple times throughout treatment for example by using ecological momentary assessments. Relatedly, although there are numerous approaches to measure pain-related avoidance in the experimental setting, avoidance is often measured through self-reports in clinical trials. These self-reports of avoidance sometimes do not reflect actual avoidance when measured through behavioral approaches (Fricke and Vogel, 2020), indicating that individuals may be unaware of their own avoidance behavior. In fact, only few studies have assessed avoidance behavior (tendencies) in itch and fatigue using other methods such as behavioral tasks (Etty et al., 2022; Heins et al., 2013; Nadinda et al., 2023). Further research is needed to develop and improve ecologically valid measures of avoidance behavior in everyday life, such as by using physiological and sensor data to measure movement (e.g., Thomas and France, 2007; Trost et al., 2012; Vitali et al., 2022). These methods would allow for more dynamic and potentially more accurate evaluation on the long-term effects of expectations and avoidance on somatic symptoms.

All in all, addressing these challenges could provide a foundation for developing and improving treatments for chronic somatic symptoms (e.g., Gatzounis et al., 2021; Kleine-Borgmann et al., 2019). For example, studies have demonstrated that placebo manipulations can improve fatigue and motor performance in healthy participants (Carlino et al., 2014; Piedimonte et al., 2015) as well as those with Parkinsons (Benedetti, 2008). Additionally, cognitive behavioral therapy and cognitive functional therapy has been shown to reduce pain-related fear-avoidance beliefs (Caneiro et al., 2017; Linden et al., 2014; Lohnberg, 2007) and disability (Schemer et al., 2019; Urits et al., 2019), and counterconditioning

and extinction techniques have been shown to reduce pain-related nocebo effects and fear (Karacaoglu et al., 2023; Meijer et al., 2023; Meulders et al., 2015; Thomaidou et al., 2020), itch-related nocebo effects (Bartels et al., 2017), as well as anxiety-related avoidance behavior (Hulsman et al., 2024). Thus, a reasonable next step may be to expand existing treatments that already target expectancies and avoidance behaviors. Specifically, exposure therapy has already shown promising results in reducing pain and fatigue (Clark and White, 2005; den Hollander et al., 2016; Sharpe et al., 2017; Simons et al., 2020; Woods and Asmundson, 2008). Exposure therapy works by exposing patients to behaviors and stimuli that they have been avoiding because of expected harm or symptoms. In the field of psychopathology, there is evidence that greater expectancy violations (overpredictions) leads to faster development of more functional behaviors during exposure therapy in children with obsessive compulsive disorders (Guzick et al., 2020). The same is likely to be true in chronic somatic symptoms. Indeed, a recent simulation study has shown that exposure therapy is effective in reducing pain because it tries to reduce the precision of (incorrect) expectancies and increase the precision of (safe) sensory input (Eckert et al., 2022). Therefore, further knowledge of how we can change expectancies to reduce dysfunctional avoidance behavior could produce even stronger effects and may lead to the development of new cost-effective interventions that may yield fewer side effects than pharmacological treatments. In fact, some researchers have already started developing treatments that combine existing therapies to better target expectancies and some behavioral components of pain, namely pain neuroscience education (Louw et al., 2016), pain reprocessing therapy (Ashar et al., 2022) and emotional awareness and expression therapy (Lumley and Schubiner, 2019) all of which have been proven to help with pain. If these components are effective, future studies can apply these treatment strategies to other chronic somatic conditions like itch, fatigue, dyspnea, and nausea.

## 7. CONCLUSION

In this article, we have described how the interaction between expectancies and avoidance can contribute to chronic pain, itch, and fatigue. We have illustrated that the two mechanisms should be evaluated together, as avoidance both occurs because of expectancies and produces new (dysfunctional) expectancies. Furthermore, using the predictive coding and active inference perspective, we have explained how our expectations are updated, and how our decision to avoid is influenced by prior experiences and sensory input. However, most studies so far have investigated the effects of expectancy and avoidance learning as two separate mechanisms. This highlights the need for more empirical research that utilizes an integrated

approach including various factors at play, such as a network approach. Additionally, further studies are needed to evaluate these transdiagnostic mechanisms in various symptoms, including itch, fatigue, and other common chronic somatic symptoms with suboptimal treatment options. If similar mechanisms are at play in various somatic symptoms, the expectancy-avoidance model can be used to further strengthen the effectiveness of existing treatment methods that can be applied to a range of somatic conditions.

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## REFERENCES

- Adamczyk, W.M., Wiercioch-Kuzianik, K., Bajcar, E.A., Bąbel, P., 2019. Rewarded placebo analgesia: a new mechanism of placebo effects based on operant conditioning. *Eur. J. Pain* 23, 923–935. <https://doi.org/10.1002/ejp.1360>.
- Ainley, V., Apps, M.A., Fotopoulou, A., Tsakiris, M., 2016. ‘Bodily precision’: a predictive coding account of individual differences in interoceptive accuracy. *Philos. Trans. R. Soc. B Biol. Sci.* 371, 20160003. <https://doi.org/10.1098/rstb.2016.0003>.
- Ashar, Y.K., Gordon, A., Schubiner, H., Uipi, C., Knight, K., Anderson, Z., Carlisle, J., Polisky, L., Geuter, S., Flood, T.F., Kragel, P.A., Dimidjian, S., Lumley, M.A., Wager, T.D., 2022. effect of pain reprocessing therapy vs placebo and usual care for patients with chronic back pain: a randomized clinical trial. *JAMA Psychiatry* 79, 13–23. <https://doi.org/10.1001/jamapsychiatry.2021.2669>.
- Aslaksen, P.M., Lyby, P.S., 2015. Fear of pain potentiates placebo hyperalgesia. *J. Pain Res.* 8, 703–710. <https://doi.org/10.2147/JPR.S91923>.
- Barrett, L.F., Simmons, W.K., 2015. Interoceptive predictions in the brain. *Nat. Rev. Neurosci.* 16, 419–429. <https://doi.org/10.1038/nrn3950>.
- Bartels, D.J.P., van Laarhoven, A.I.M., Stroo, M., Hijne, K., Peerdeman, K.J., Donders, A.R.T., van de Kerkhof, P.C.M., Evers, A.W.M., 2017. Minimizing placebo effects by conditioning with verbal suggestion: a randomized clinical trial in healthy humans. *PLOS ONE* 12, e0182959. <https://doi.org/10.1371/journal.pone.0182959>.
- Benedetti, F., 2008. Mechanisms of placebo and placebo-related effects across diseases and treatments. *Annu. Rev. Pharmacol. Toxicol.* 48, 33–60. <https://doi.org/10.1146/annurev.pharmtox.48.113006.094711>.
- Blasini, M., Corsi, N., Klinger, R., Colloca, L., 2017. Nocebo and pain: an overview of the psychoneurobiological mechanisms. *Pain Rep.* 2. <https://doi.org/10.1097/PR9.0000000000000585>
- Blythe, J.S., Peerdeman, K.J., Veldhuijzen, D.S., van Laarhoven, A.I.M., Evers, A.W.M., 2019. Placebo and nocebo effects on itch: a review of experimental methods. *Itch* 4, e27–e27. <https://doi.org/10.1097/itr.0000000000000027>.
- 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, 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. *J. Behav. Med.* 33, 355–363. <https://doi.org/10.1007/s10865-010-9266-8>.
- Bonnert, M., Olén, O., Bjureberg, J., Lalouni, M., Hedman-Lagerlöf, E., Serlachius, E., Ljótsson, B., 2018. The role of avoidance behavior in the treatment of adolescents with irritable bowel syndrome: a mediation analysis. *Behav. Res. Ther.* 105, 27–35. <https://doi.org/10.1016/j.brat.2018.03.006>.
- Bottoms, L., Buscombe, R., Nicholettos, A., 2014. The placebo and nocebo effects on peak minute power during incremental arm crank ergometry. *Eur. J. Sport Sci.* 14, 362–367. <https://doi.org/10.1080/17461391.2013.822564>.
- Boullosa, D.A., Nakamura, F.Y., 2013. The evolutionary significance of fatigue. *Front.*

- Physiol. 4, 309. <https://doi.org/10.3389/fphys.2013.00309>.
- Broelz, E.K., Wolf, S., Schneeweiss, P., Niess, A.M., Enck, P., Weimer, K., 2018. Increasing effort without noticing: a randomized controlled pilot study about the ergogenic placebo effect in endurance athletes and the role of supplement salience. *PloS One* 13, e0198388. <https://doi.org/10.1371/journal.pone.0198388>.
- Büchel, C., Geuter, S., Sprenger, C., Eippert, F., 2014. Placebo analgesia: a predictive coding perspective. *Neuron* 81, 1223–1239. <https://doi.org/10.1016/j.neuron.2014.02.042>.
- Caneiro, J.P., Smith, A., Rabey, M., Moseley, G.L., O’Sullivan, P., 2017. Process of change in pain-related fear: clinical insights from a single case report of persistent back pain managed with cognitive functional therapy. *J. Orthop. Sports Phys. Ther.* 47, 637–651. <https://doi.org/10.2519/jospt.2017.7371>.
- Carlino, E., Benedetti, F., Pollo, A., 2014. The effects of manipulating verbal suggestions on physical performance. *Z. F. üR. Psychol.* 222, 154–164. <https://doi.org/10.1027/2151-2604/a000178>.
- Carriere, J.S., Thibault, P., Milioto, M., Sullivan, M.J.L., 2015. Expectancies mediate the relations among pain catastrophizing, fear of movement, and return to work outcomes after whiplash injury. *J. Pain* 16, 1280–1287. <https://doi.org/10.1016/j.jpain.2015.09.001>.
- Cevikbas, F., Lerner, E.A., 2020. Physiology and pathophysiology of itch. *Physiol. Rev.* 100, 945–982. <https://doi.org/10.1152/physrev.00017.2019>.
- Claes, N., Crombez, G., Vlaeyen, J.W.S., 2015. Pain-avoidance versus reward-seeking: an experimental investigation. *Pain* 156, 1449–1457. <https://doi.org/10.1097/j.pain.000000000000116>.
- Claes, N., Karos, K., Meulders, A., Crombez, G., Vlaeyen, J.W.S., 2014. competing goals attenuate avoidance behavior in the context of pain. *J. Pain* 15, 1120–1129. <https://doi.org/10.1016/j.jpain.2014.08.003>.
- Clark, L.V., White, P.D., 2005. The role of deconditioning and therapeutic exercise in chronic fatigue syndrome (CFS). *J Ment Health* 14, 237–252. <https://doi.org/10.1080/09638230500136308>.
- Cole, E., Yeung, H., Chen, S., 2021. The quality of life impact of chronic itch compared to pain, in: Yosipovitch, G., Andersen, H.H., Arendt-Nielsen, L. (Eds.), *Itch and Pain: Similarities, Interactions, and Differences*. Wolters Kluwer, Philadelphia, pp. 10–21.
- Crombez, G., Eccleston, C., Van Damme, S., Vlaeyen, J.W.S., Karoly, P., 2012. Fear-avoidance model of chronic pain: the next generation. *Clin. J. Pain* 28, 475–483. <https://doi.org/10.1097/AJP.0b013e3182385392>.
- Dahlhamer, J., Lucas, J., Zelaya, C., Nahin, R., Mackey, S., DeBar, L., Kerns, R., Von Korff, M., Porter, L., Helmick, C., 2018. Prevalence of chronic pain and high-impact chronic pain among adults—United States, 2016. *Morb. Mortal. Wkly. Rep.* 67, 1001. <https://doi.org/10.15585/mmwr.mm6736a2>.
- Di Lernia, D., Serino, S., Riva, G., 2016. Pain in the body. Altered interoception in chronic pain conditions: A systematic review. *Neurosci. Biobehav. Rev.* 71, 328–341. <https://doi.org/10.1016/j.neubiorev.2016.09.015>.
- Eccles, J.A., Davies, K.A., 2021. The challenges of chronic pain and fatigue. *Clin. Med.* 21, 19. <https://doi.org/10.7861/clinmed.2020-1009>.
- Eckert, A.-L., Pabst, K., Endres, D.M., 2022. A Bayesian model for chronic pain. *Front. Pain Res.* 3. <https://doi.org/10.3389/fpain.2022.966034>.

- Etty, S., George, D.N., Van Laarhoven, A.I., Holle, H., 2022. Acute itch induces attentional avoidance of itch-related information. *Acta Derm. Venereol.* <https://doi.org/10.2340/actadv.v102.1626>.
- Evers, A.W.M., Peerdeman, K.J., Laarhoven, A.I.M., 2019. What is new in the psychology of chronic itch? *Exp. Dermatol.* 28, 6. <https://doi.org/10.1111/exd.13992>.
- Feldman, H., Friston, K., 2010. Attention, uncertainty, and free-energy. *Front. Hum. Neurosci.* 4. <https://doi.org/10.3389/fnhum.2010.00215>.
- Fricke, K., Vogel, S., 2020. How interindividual differences shape approach-avoidance behavior: Relating self-report and diagnostic measures of interindividual differences to behavioral measurements of approach and avoidance. *Neurosci. Biobehav. Rev.* 111, 30–56. <https://doi.org/10.1016/j.neubiorev.2020.01.008>.
- Friston, K., 2010. The free-energy principle: a unified brain theory? *Nat. Rev. Neurosci.* 11, 127–138. <https://doi.org/10.1038/nrn2787>.
- Friston, K., FitzGerald, T., Rigoli, F., Schwartenbeck, P., O'Doherty, J., Pezzulo, G., 2016. Active inference and learning. *Neurosci. Biobehav. Rev.* 68, 862–879. <https://doi.org/10.1016/j.neubiorev.2016.06.022>.
- Friston, K., FitzGerald, T., Rigoli, F., Schwartenbeck, P., Pezzulo, G., 2017. Active inference: a process theory. *Neural Comput.* 29, 1–49. [https://doi.org/10.1162/NECO\\_a\\_00912](https://doi.org/10.1162/NECO_a_00912).
- Froehlich, L., Hattesohl, D.B., Cotler, J., Jason, L.A., Scheibenbogen, C., Behrends, U., 2022. Causal attributions and perceived stigma for myalgic encephalomyelitis/chronic fatigue syndrome. *J. Health Psychol.* 27, 2291–2304. <https://doi.org/10.1177/13591053211027631>.
- Gatzounis, R., den Hollander, M., Meulders, A., 2021. Optimizing long-term outcomes of exposure for chronic primary pain from the lens of learning theory. *J. Pain* 22, 1315–1327. <https://doi.org/10.1016/j.jpain.2021.04.012>.
- Gerbershagen, H.U., Lindena, G., Korb, J., Kramer, S., 2002. Health-related quality of life in patients with chronic pain. *Schmerz Berl. Ger.* 16, 271–284. <https://doi.org/10.1007/s00482-002-0164-z>.
- Griffiths, T.L., Kemp, C., Tenenbaum, J.B., 2008. Bayesian models of cognition. *Camb. Handb. Comput. Model.* 1–49. <https://doi.org/10.1017/CBO9780511816772.006>.
- Guzick, A.G., Reid, A.M., Balkhi, A.M., Geffken, G.R., McNamara, J.P., 2020. That was easy! expectancy violations during exposure and response prevention for childhood obsessive-compulsive disorder. *Behav. Modif.* 44, 319–342. <https://doi.org/10.1177/0145445518813624>.
- Harvey, A., Watkins, E., Mansell, W., Shafran, R., 2004. Cognitive behavioural processes across psychological disorders: A transdiagnostic approach to research and treatment, *Cognitive Behavioural Processes across Psychological Disorders*. Oxford University Press.
- Hedman-Lagerlöf, M., Andersson, E., Hedman-Lagerlöf, E., Wicksell, R.K., Flink, I., Ljótsson, B., 2019. Approach as a key for success: Reduced avoidance behaviour mediates the effect of exposure therapy for fibromyalgia. *Behav. Res. Ther.* 122, 103478. <https://doi.org/10.1016/j.brat.2019.103478>.
- Heins, M., Knoop, H., Nijs, J., Feskens, R., Meeus, M., Moorkens, G., Bleijenberg, G., 2013. Influence of symptom expectancies on stair-climbing performance in chronic fatigue syndrome: effect of study context. *Int. J. Behav. Med.* 20, 213–218. <https://doi.org/10.1007/s12529-012-9253-2>.

- Hohwy, J., 2017. Priors in perception: top-down modulation, Bayesian perceptual learning rate, and prediction error minimization. *Conscious. Cogn., Cogn. Penetration Predict. Coding* 47, 75–85. <https://doi.org/10.1016/j.concog.2016.09.004>.
- den Hollander, M., Goossens, M., de Jong, J., Ruijgrok, J., Oosterhof, J., Onghena, P., Smeets, R., Vlaeyen, J.W.S., 2016. Expose or protect? A randomized controlled trial of exposure in vivo vs pain-contingent treatment as usual in patients with complex regional pain syndrome type 1. *PAIN* 157, 2318–2329. <https://doi.org/10.1097/j.pain.0000000000000651>.
- Hulsman, A.M., van de Pavert, I., Roelofs, K., Klumpers, F., 2024. Tackling costly fearful avoidance using pavlovian counterconditioning. *Behav. Ther.* 55, 361–375. <https://doi.org/10.1016/j.beth.2023.07.013>.
- Janssens, T., Meulders, A., Cuyvers, B., Colloca, L., Vlaeyen, J.W.S., 2019. Placebo and nocebo effects and operant pain-related avoidance learning. *PAIN Rep.* 4, e748. <https://doi.org/10.1097/PR9.0000000000000748>.
- Jepma, M., Roy, M., Ramlakhan, K., Van Velzen, M., Dahan, A., 2022. Different brain systems support learning from received and avoided pain during human pain-avoidance learning. *eLife* 11, e74149. <https://doi.org/10.7554/eLife.74149>.
- de Jong, P.J., Daniels, J.K., 2020. Chapter 4 - Negative expectancy biases in psychopathology, in: Aue, T., Okon-Singer, H. (Eds.), *Cognitive Biases in Health and Psychiatric Disorders*. Academic Press, pp. 71–97. <https://doi.org/10.1016/B978-0-12-816660-4.00004-0>.
- Jungilligens, J., Paredes-Echeverri, S., Popkirov, S., Barrett, L. F., Perez, D. L. (2022). A new science of emotion: implications for functional neurological disorder. *Brain*, 145(8), 2648–2663. <https://doi.org/10.1093/brain/awac204>.
- Karacaoglu, M., Meijer, S., Peerdeman, K.J., Dusseldorp, E., Jensen, K.B., Veldhuijzen, D.S., van Middendorp, H., Evers, A.W.M., 2023. Susceptibility to nocebo hyperalgesia, dispositional optimism, and trait anxiety as predictors of nocebo hyperalgesia reduction. *Clin. J. Pain* 39, 259–269. <https://doi.org/10.1097/AJP.0000000000001112>.
- Kirsch, I., 1985. Response expectancy as a determinant of experience and behavior. *Am. Psychol.* 14. <https://doi.org/10.1037/0003-066X.40.11.1189>.
- Kirsch, I., 1997. Response expectancy theory and application: a decennial review. *Appl. Prev. Psychol.* 6, 69–79. [https://doi.org/10.1016/S0962-1849\(05\)80012-5](https://doi.org/10.1016/S0962-1849(05)80012-5).
- Kirsch, I., 2018. Chapter Five - Response Expectancy and the Placebo Effect, in: Colloca, L. (Ed.), *International Review of Neurobiology, Neurobiology of the Placebo Effect Part I*. Academic Press, pp. 81–93. <https://doi.org/10.1016/bs.irn.2018.01.003>.
- Kiverstein, J., Kirchhoff, M.D., Thacker, M., 2022. An embodied predictive processing theory of pain experience. *Rev. Philos. Psychol.* 13, 973–998. <https://doi.org/10.1007/s13164-022-00616-2>.
- Kleine-Borgmann, J., Schmidt, K., Hellmann, A., Bingel, U., 2019. Effects of open-label placebo on pain, functional disability, and spine mobility in patients with chronic back pain: a randomized controlled trial. *PAIN* 160, 2891–2897. <https://doi.org/10.1097/j.pain.0000000000001683>.
- Knoop, H., Prins, J.B., Moss-Morris, R., Bleijenberg, G., 2010. The central role of cognitive processes in the perpetuation of chronic fatigue syndrome. *J. Psychosom. Res., Funct. Somat. Syndr.* 68, 489–494. <https://doi.org/10.1016/j.jpsychores.2010.01.022>.

- Kroska, E.B., 2016. A meta-analysis of fear-avoidance and pain intensity: the paradox of chronic pain. *Scand. J. Pain* 13, 43–58. <https://doi.org/10.1016/j.sjpain.2016.06.011>.
- Kube, T., Rozenkrantz, L., Rief, W., Barsky, A., 2020. Understanding persistent physical symptoms: conceptual integration of psychological expectation models and predictive processing accounts. *Clin. Psychol. Rev.* 76, 101829. <https://doi.org/10.1016/j.cpr.2020.101829>.
- van Laarhoven, A.I.M., van der Sman-Mauriks, I.M., Donders, A.R.T., Pronk, M.C., van de Kerkhof, P.C.M., Evers, A.W.M., 2015. Placebo effects on itch: a meta-analysis of clinical trials of patients with dermatological conditions. *J. Invest. Dermatol.* 135, 1234–1243. <https://doi.org/10.1038/jid.2014.522>.
- Lenaert, B., Boddez, Y., Vlaeyen, J.W., van Heugten, C.M., 2018. Learning to feel tired: a learning trajectory towards chronic fatigue. *Behav. Res. Ther.* 100, 54–66. <https://doi.org/10.1016/j.brat.2017.11.004>.
- Lersch, F.E., Frickmann, F.C.S., Urman, R.D., Burgermeister, G., Siercks, K., Luedi, M.M., Straumann, S., 2023. Analgesia for the bayesian brain: how predictive coding offers insights into the subjectivity of pain. *Curr. Pain Headache Rep.* 27, 631–638. <https://doi.org/10.1007/s11916-023-01122-5>.
- Lethem, J., Slade, P., Troup, J.D.G., Bentley, G., 1983. Outline of a fear-avoidance model of exaggerated pain perception.1. *Behav. Res. Ther.* 21, 401–8. [https://doi.org/10.1016/0005-7967\(83\)90009-8](https://doi.org/10.1016/0005-7967(83)90009-8).
- Lim, E.-J., Ahn, Y.-C., Jang, E.-S., Lee, S.-W., Lee, S.-H., Son, C.-G., 2020. Systematic review and meta-analysis of the prevalence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). *J. Transl. Med.* 18, 100. <https://doi.org/10.1186/s12967-020-02269-0>.
- Linden, M., Scherbe, S., Cicholas, B., 2014. Randomized controlled trial on the effectiveness of cognitive behavior group therapy in chronic back pain patients. *J. Back Musculoskelet. Rehabil.* 27, 563–568. <https://doi.org/10.3233/BMR-140518>.
- Linton, S.J., 2013. A transdiagnostic approach to pain and emotion. *J. Appl. Biobehav. Res.* 18, 82–103. <https://doi.org/10.1111/jabr.12007>.
- Locatelli, G., Matus, A., James, R., Salmoiraghi, Blotcher, E., Ausili, D., Vellone, E., Riegel, B., 2023. What is the role of interoception in the symptom experience of people with a chronic condition? A systematic review. *Neurosci. Biobehav. Rev.* 148, 105142. <https://doi.org/10.1016/j.neubiorev.2023.105142>.
- Lohnberg, J.A., 2007. A review of outcome studies on cognitive-behavioral therapy for reducing fear-avoidance beliefs among individuals with chronic pain. *J. Clin. Psychol. Med. Settings* 14, 113–122. <https://doi.org/10.1007/s10880-007-9062-y>.
- Louw, A., Zimney, K., Puenteadura, E.J., Diener, I., 2016. The efficacy of pain neuroscience education on musculoskeletal pain: a systematic review of the literature. *Physiother. Theory Pract.* 32, 332–355. <https://doi.org/10.1080/09593985.2016.1194646>.
- Lovibond, P., 2006. Fear and Avoidance: An Integrated Expectancy Model., in: Craske, M.G., Hermans, D., Vansteenwegen, D. (Eds.), *Fear and Learning: From Basic Processes to Clinical Implications*. American Psychological Association, Washington, pp. 117–132. <https://doi.org/10.1037/11474-006>.
- Lumley, M.A., Schubiner, H., 2019. Emotional awareness and expression therapy for chronic pain: rationale, principles and techniques, evidence, and critical review.

- Curr. Rheumatol. Rep. 21, 30. <https://doi.org/10.1007/s11926-019-0829-6>.
- Maggio, J., Alluri, P.R., Paredes-Echeverri, S., Larson, A.G., Sojka, P., Price, B.H., Aybek, S., Perez, D.L., 2020. Briquet syndrome revisited: implications for functional neurological disorder. *Brain Commun.* 2, fcaa156. <https://doi.org/10.1093/braincomms/fcaa156>.
- Maisto, D., Barca, L., Van den Bergh, O., Pezzulo, G., 2021. Perception and misperception of bodily symptoms from an active inference perspective: modelling the case of panic disorder. *Psychol. Rev.* 128, 690–710. <https://doi.org/10.1037/rev0000290>.
- Marks, M., de Silva, P., 1994. The ‘match/mismatch’ model of fear: empirical status and clinical implications. *Behav. Res. Ther.* 32, 759–770. [https://doi.org/10.1016/0005-7967\(94\)90034-5](https://doi.org/10.1016/0005-7967(94)90034-5).
- Marlow, L.L., Faull, O.K., Finnegan, S.L., Pattinson, K.T.S., 2019. Breathlessness and the brain: the role of expectation. *Curr. Opin. Support. Palliat. Care* 13, 200. <https://doi.org/10.1097/SPC.0000000000000441>.
- Meijer, S., Karacaoglu, M., van Middendorp, H., Veldhuijzen, D.S., Jensen, K.B., Peerdeman, K.J., Evers, A.W.M., 2023. Efficacy of open-label counterconditioning for reducing nocebo effects on pressure pain. *Eur. J. Pain Lond. Engl.* 27, 831–847. <https://doi.org/10.1002/ejp.2112>.
- Meissner, K., Bingel, U., Colloca, L., Wager, T.D., Watson, A., Flaten, M.A., 2011. The placebo effect: advances from different methodological approaches. *J. Neurosci.* 31, 16117–16124. <https://doi.org/10.1523/JNEUROSCI.4099-11.2011>.
- Mense, S., Schiltenswolf, M., 2010. Fatigue and pain; what is the connection? *Pain* 148, 177–178. <https://doi.org/10.1016/j.pain.2009.11.010>.
- Meulders, A., 2019. From fear of movement-related pain and avoidance to chronic pain disability: a state-of-the-art review. *Curr. Opin. Behav. Sci.* 26, 130–136. <https://doi.org/10.1016/j.cobeha.2018.12.007>.
- Meulders, A., Karsdorp, P.A., Claes, N., Vlaeyen, J.W.S., 2015. Comparing counterconditioning and extinction as methods to reduce fear of movement-related pain. *J. Pain* 16, 1353–1365. <https://doi.org/10.1016/j.jpain.2015.09.007>.
- Milde, C., Brinskelle, L.S., Glombiewski, J.A., 2024. Does active inference provide a comprehensive theory of placebo analgesia? *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* 9, 10–20. <https://doi.org/10.1016/j.bpsc.2023.08.007>.
- Morrison, I., 2013. Facets and mechanisms of adaptive pain behavior: predictive regulation and action. *Front. Hum. Neurosci.* 7. <https://doi.org/10.3389/fnhum.2013.00755>.
- Mowrer, O.H., 1951. Two-factor learning theory: summary and comment. *Psychol. Rev.* 58, 350–354. <https://doi.org/10.1037/h0058956>.
- Nadinda, P.G., van Laarhoven, A.I.M., Evers, A.W.M., Maas, J., van Beugen, S., 2023. Itch-related avoidance and attentional biases in patients with psoriasis? *J. Invest. Dermatol.* 143, 1848–1850.e8. <https://doi.org/10.1016/j.jid.2023.02.032>.
- Nicholas, M. k., Asghari, A., Sharpe, L., Brnabic, A., Wood, B. m., Overton, S., Tonkin, L., de Sousa, M., Finniss, D., Beeston, L., Sutherland, A., Corbett, M., Brooker, C., 2014. Cognitive exposure versus avoidance in patients with chronic pain: adherence matters. *Eur. J. Pain* 18, 424–437. <https://doi.org/10.1002/j.1532-2149.2013.00383.x>.
- Oka, T., 2013. Influence of psychological stress on chronic fatigue syndrome. *Adv. Neuroimmune Biol.* 4, 301–309. <https://doi.org/10.3233/NIB-130077>.

- 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. *Front. Psychol.* 7. <https://doi.org/10.3389/fpsyg.2016.01270>.
- Peiffer, C., 2023. Puzzled by dysfunctional breathing disorder(s)? Consider the Bayesian brain hypothesis! *Front. Neurosci.* 17. <https://doi.org/10.3389/fnins.2023.1270556>.
- Perugino, F., De Angelis, V., Pompili, M., Martelletti, P., 2022. Stigma and Chronic Pain. *Pain Ther.* 11, 1085–1094. <https://doi.org/10.1007/s40122-022-00418-5>.
- Petersen, M.W., Schröder, A., Jørgensen, T., Ørnbøl, E., Meinertz Dantoft, T., Eliassen, M., Benros, M.E., Fink, P., 2020. Irritable bowel, chronic widespread pain, chronic fatigue and related syndromes are prevalent and highly overlapping in the general population: DanFunD. *Sci. Rep.* 10, 1–10. <https://doi.org/10.1038/s41598-020-60318-6>.
- Pezzulo, G., 2014. Why do you fear the bogeyman? An embodied predictive coding model of perceptual inference. *Cogn. Affect. Behav. Neurosci.* 14, 902–911. <https://doi.org/10.3758/s13415-013-0227-x>.
- Pezzulo, G., Maisto, D., Barca, L., Bergh, O.V. den, 2019. Symptom perception from a predictive processing perspective. *Clin. Psychol. Eur.* 1, 1–14. <https://doi.org/10.32872/cpe.v1i4.35952>.
- Philips, H.C., 1987. Avoidance behaviour and its role in sustaining chronic pain. *Behav. Res. Ther.* 25, 273–279. [https://doi.org/10.1016/0005-7967\(87\)90005-2](https://doi.org/10.1016/0005-7967(87)90005-2).
- Picon, E.L., Perez, D.L., Burke, M.J., Debert, C.T., Iverson, G.L., Panenka, W.J., Silverberg, N.D., 2021. Unexpected symptoms after concussion: potential links to functional neurological and somatic symptom disorders. *J. Psychosom. Res.* 151, 110661. <https://doi.org/10.1016/j.jpsychores.2021.110661>.
- Piedimonte, A., Benedetti, F., Carlino, E., 2015. Placebo-induced decrease in fatigue: evidence for a central action on the preparatory phase of movement. *Eur. J. Neurosci.* 41, 492–497. <https://doi.org/10.1111/ejn.12806>.
- Pittig, A., Wong, A.H.K., Glück, V.M., Boschet, J.M., 2020. Avoidance and its bi-directional relationship with conditioned fear: mechanisms, moderators, and clinical implications. *Behav. Res. Ther.* 126, 103550. <https://doi.org/10.1016/j.brat.2020.103550>.
- Rachman, S., Arntz, A., 1991. The overprediction and underprediction of pain. *Clin. Psychol. Rev.* 11, 339–355. [https://doi.org/10.1016/0272-7358\(91\)90112-8](https://doi.org/10.1016/0272-7358(91)90112-8).
- Reed, D.E., Cobos, B., Nagpal, A.S., Eckmann, M., McGeary, D.D., 2022. The role of identity in chronic pain cognitions and pain-related disability within a clinical chronic pain population. *Int. J. Psychiatry Med.* 57, 35–52. <https://doi.org/10.1177/0091217421989141>.
- Rief, W., Glombiewski, J.A., Gollwitzer, M., Schubö, A., Schwarting, R., Thorwart, A., 2015. Expectancies as core features of mental disorders. *Curr. Opin. Psychiatry* 28, 378–385. <https://doi.org/10.1097/YCO.0000000000000184>.
- Roefs, A., Fried, E.I., Kindt, M., Martijn, C., Elzinga, B., Evers, A.W.M., Wiers, R.W., Borsboom, D., Jansen, A., 2022. A new science of mental disorders: using personalised, transdiagnostic, dynamical systems to understand, model, diagnose and treat psychopathology. *Behav. Res. Ther.* 153, 104096. <https://doi.org/10.1016/j.brat.2022.104096>.
- Ruscheweyh, R., Pereira, D., Hasenbring, M.I., Straube, A., 2019. Pain-related avoidance and endurance behaviour in migraine: an

- observational study. *J. Headache Pain* 20, 9. <https://doi.org/10.1186/s10194-019-0962-7>.
- Sanders, K.M., Akiyama, T., 2018. The vicious cycle of itch and anxiety. *Neurosci. Biobehav. Rev.* 87, 17–26. <https://doi.org/10.1016/j.neubiorev.2018.01.009>.
- Schemer, L., Schroeder, A., Ørnbøl, E., Glombiewski, J.A., 2019. Exposure and cognitive-behavioural therapy for chronic back pain: an RCT on treatment processes. *Eur. J. Pain* 23, 526–538. <https://doi.org/10.1002/ejp.1326>.
- Seligman, M.E., Johnston, J.C., 1973. A cognitive theory of avoidance learning., in: McGuigan, F.J., Lumsden, D.B. (Eds.), *Contemporary Approaches to Conditioning and Learning*. Winston and Sons, Washington, DC, pp. 69–110.
- Sharpe, M., Chalder, T., Johnson, A.L., Goldsmith, K.A., White, P.D., 2017. Do more people recover from chronic fatigue syndrome with cognitive behaviour therapy or graded exercise therapy than with other treatments? *Fatigue Biomed. Health Behav.* 5, 57–61. <https://doi.org/10.1080/21641846.2017.1288629>.
- 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. *Am. J. Clin. Dermatol.* 19, 759–769. <https://doi.org/10.1007/s40257-018-0381-6>.
- Simons, L., Vlaeyen, J.W.S., Declercq, L., Smith, A., Beebe, J., Hogan, M., Li, E., Kronman, C., Mahmud, F., Corey, J., Sieberg, C., Ploski, C., 2020. Avoid or engage? Outcomes of graded exposure in youth with chronic pain using a sequential replicated single-case randomized design. *Pain* 161, 520–531. <https://doi.org/10.1097/j.pain.0000000000001735>.
- Smith, R., Friston, K.J., Whyte, C.J., 2022. A step-by-step tutorial on active inference and its application to empirical data. *J. Math. Psychol.* 107, 102632.
- Snell, D.L., Faulkner, J.W., Williman, J.A., Silverberg, N.D., Theadom, A., Surgenor, L.J., Hackney, J., Siegert, R.J., 2023. Fear avoidance and return to work after mild traumatic brain injury. *Brain Inj.* 37, 541–550. <https://doi.org/10.1080/02699052.2023.2180663>.
- Tabor, A., Burr, C., 2019. Bayesian learning models of pain: a call to action. *Curr. Opin. Behav. Sci.* 26, 54–61. <https://doi.org/10.1016/j.cobeha.2018.10.006>.
- 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. *Psychosom. Med.* 85, 308–321. <https://doi.org/10.1097/PSY.0000000000001194>.
- Thomaidou, M.A., Veldhuijzen, D.S., Peerdeman, K.J., Wiebing, N.Z.S., Blythe, J.S., Evers, A.W.M., 2020. Learning mechanisms in nocebo hyperalgesia: the role of conditioning and extinction processes. *Pain* 161, 1597–1608. <https://doi.org/10.1097/j.pain.0000000000001861>.
- Thomas, J.S., France, C.R., 2007. Pain-related fear is associated with avoidance of spinal motion during recovery from low back pain. *Spine* 32, E460. <https://doi.org/10.1097/BRS.0b013e3180bc1f7b>.
- Thompson, E.L., Broadbent, J., Fuller-Tyszkiewicz, M., Bertino, M.D., Staiger, P.K., 2019. A network analysis of the links between chronic pain symptoms and affective disorder symptoms. *Int. J. Behav. Med.* 26, 59–68. <https://doi.org/10.1007/s12529-018-9754-8>.

- Tolman, E.C., 1948. Cognitive maps in rats and men. *Psychol. Rev.* 55, 189–208. <https://doi.org/10.1037/h0061626>.
- Trost, Z., France, C.R., Sullivan, M.J., Thomas, J.S., 2012. Pain-related fear predicts reduced spinal motion following experimental back injury. *PAIN* 153, 1015–1021. <https://doi.org/10.1016/j.pain.2012.02.001>.
- Urits, I., Hubble, A., Peterson, E., Orhurhu, V., Ernst, C.A., Kaye, A.D., Viswanath, O., 2019. An update on cognitive therapy for the management of chronic pain: a comprehensive review. *Curr. Pain Headache Rep.* 23, 57. <https://doi.org/10.1007/s11916-019-0794-9>.
- Van Damme, S., Van Ryckeghem, D.M.L., Wyffels, F., Van Hulle, L., Crombez, G., 2012. No pain no gain? Pursuing a competing goal inhibits avoidance behavior. *PAIN* 153, 800–804. <https://doi.org/10.1016/j.pain.2011.12.015>.
- Van den Bergh, O., Brosschot, J., Critchley, H., Thayer, J.F., Ottaviani, C., 2021. Better safe than sorry: a common signature of general vulnerability for psychopathology. *Perspect. Psychol. Sci. J. Assoc. Psychol. Sci.* 16, 225–246. <https://doi.org/10.1177/1745691620950690>.
- Van den Bergh, O., Witthöft, M., Petersen, S., Brown, R.J., 2017. Symptoms and the body: taking the inferential leap. *Neurosci. Biobehav. Rev.* 74, 185–203. <https://doi.org/10.1016/j.neubiorev.2017.01.015>.
- Van Heck, G.L., de Vries, J., 2002. Quality of life of patients with chronic fatigue syndrome. *J. Chronic Fatigue Syndr.* 10, 17–35. [https://doi.org/10.1300/J092v10n01\\_03](https://doi.org/10.1300/J092v10n01_03).
- Vase, L., Petersen, G.L., 2013. Chapter 20 - conceptualizations and magnitudes of placebo analgesia effects across meta-analyses and experimental studies, in: Colloca, L., Flaten, M.A., Meissner, K. (Eds.), *Placebo and Pain*. Academic Press, San Diego, pp. 203–213. <https://doi.org/10.1016/B978-0-12-397928-5.00020-9>.
- Verhoeven, E.W.M., Kraaimaat, F.W., Van De Kerkhof, P.C.M., Van Weel, C., Duller, P., Van Der Valk, P.G.M., Van Den Hoogen, H.J.M., Bor, J.H.J., Schers, H.J., Evers, A.W.M., 2007. Prevalence of physical symptoms of itch, pain and fatigue in patients with skin diseases in general practice. *Br. J. Dermatol.* 156, 1346–1349. <https://doi.org/10.1111/j.1365-2133.2007.07916.x>.
- Vitali, D., Olugbade, T., Eccleston, C., Keogh, E., Bianchi-Berthouze, N., de C Williams, A.C., 2022. Sensing behavior change in chronic pain: a scoping review of sensor technology for use in daily life. *Pain* 10.1097/j.pain.0000000000003134. <https://doi.org/10.1097/j.pain.0000000000003134>.
- Vlaeyen, J.W.S., Crombez, G., Linton, S.J., 2016. The fear-avoidance model of pain. *Pain* 157, 1588–1589. <https://doi.org/10.1097/j.pain.0000000000000574>.
- Vlaeyen, J.W.S., Crombez, G., 2020. Behavioral conceptualization and treatment of chronic pain. *Annu. Rev. Clin. Psychol.* 16, 187–212. <https://doi.org/10.1146/annurev-clinpsy-050718-095744>.
- Vlaeyen, J.W.S., Haslbeck, J.M.B., Sjouwerman, R., Peters, M.L., 2022. Towards a dynamic account of chronic pain. *Pain* 163, e1038. <https://doi.org/10.1097/j.pain.0000000000002706>.
- Vlaeyen, J.W.S., Kole-Snijders, A.M.J., Boeren, R.G.B., van Eek, H., 1995. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. *PAIN* 62, 363. [https://doi.org/10.1016/0304-3959\(94\)00279-N](https://doi.org/10.1016/0304-3959(94)00279-N).
- Vlaeyen, J.W.S., Linton, S.J., 2000. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain*

- 85, 317–332. [https://doi.org/10.1016/S0304-3959\(99\)00242-0](https://doi.org/10.1016/S0304-3959(99)00242-0).
- Vlaeyen, J.W.S., Linton, S.J., 2012. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. *PAIN* 153, 1144–1147. <https://doi.org/10.1016/j.pain.2011.12.009>.
- Volders, S., Boddez, Y., De Peuter, S., Meulders, A., Vlaeyen, J.W.S., 2015. Avoidance behavior in chronic pain research: A cold case revisited. *Behav. Res. Ther.* 64, 31–37. <https://doi.org/10.1016/j.brat.2014.11.003>.
- Walters, E.T., Williams, A.C. de C., 2019. Evolution of mechanisms and behaviour important for pain. *Philos. Trans. R. Soc. B Biol. Sci.* 374, 20190275. <https://doi.org/10.1098/rstb.2019.0275>.
- Warlich, B., Fritz, F., Osada, N., Bruland, P., Stumpf, A., Schneider, G., Dugas, M., Pfeleiderer, B., Ständer, S., 2015. Health-related quality of life in chronic pruritus: an analysis related to disease etiology, clinical skin conditions and itch intensity. *Dermatology* 231, 253–259. <https://doi.org/10.1159/000437206>.
- Warren, R., Zgourides, G., Jones, A., 1989. Cognitive bias and irrational belief as predictors of avoidance. *Behav. Res. Ther.* 27, 181–188. [https://doi.org/10.1016/0005-7967\(89\)90077-6](https://doi.org/10.1016/0005-7967(89)90077-6).
- Weishaar, E., 2016. Epidemiology of itch. *Curr. Probl. Dermatol.* 50, 5–10. <https://doi.org/10.1159/000446010>.
- Weng, L., van Laarhoven, A.I., Peerdeman, K.J., Evers, A.W., 2022. Induction and generalization of nocebo effects on itch. *Exp. Dermatol.* 13. <https://doi.org/10.3389/fpsyt.2022.838578>.
- Wolters, F., Peerdeman, K.J., Evers, A.W.M., 2019. Placebo and nocebo effects across symptoms: From pain to fatigue, dyspnea, nausea, and itch. *Front. Psychiatry* 10, 470. <https://doi.org/10.3389/fpsyt.2019.00470>.
- Woo, A.K., 2010. Depression and anxiety in pain. *Rev. Pain* 4, 8–12. <https://doi.org/10.1177/204946371000400103>.
- Woods, M.P., Asmundson, G.J., 2008. Evaluating the efficacy of graded in vivo exposure for the treatment of fear in patients with chronic back pain: a randomized controlled clinical trial. *Pain* 136, 271–280. <https://doi.org/10.1016/j.pain.2007.06.037>.
- Yang, J., Lo, W.L.A., Zheng, F., Cheng, X., Yu, Q., Wang, C., 2022. Evaluation of cognitive behavioral therapy on improving pain, fear avoidance, and self-efficacy in patients with chronic low back pain: a systematic review and meta-analysis. *Pain Res. Manag.* 2022, e4276175. <https://doi.org/10.1155/2022/4276175>.
- Yu, L., Norton, S., Harrison, A., McCracken, L.M., 2015. In search of the person in pain: A systematic review of conceptualization, assessment methods, and evidence for self and identity in chronic pain. *J. Context. Behav. Sci.* 4, 246–262. <https://doi.org/10.1016/j.jcbs.2015.10.003>.

