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A PAINFUL PEEK INTO THE UNDERLYING MECHANISMS OF MINDFULNESS

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Among percepts, each man is inevitably confined to his own; what he knows of the percepts of others he knows by inference from his own percepts in hearing and reading. The percepts of dreamers and madmen, as percepts, are just as good as those of others; the only objection to them is that, as their context is unusual, they are apt to give rise to fallacious inferences.

— Bertrand Russell —

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Abstract

The burgeoning scientific interest in the clinical benefits of mindfulness has resulted in an extensive body of research linking mindfulness-based practices to improvements across a wide range of pain-related outcomes. Yet, a clear understanding of the mechanisms via which mindfulness conveys its purported effects is still lacking. Novel insights from neuroimaging studies suggest that mindfulness may alleviate pain via unique neural mechanisms characterised by increased pain-related sensory processing and abatement of evaluative and memory-related processes. In light of these observations, recently formulated predictive processing accounts posit that the non-elaborative sustained attention to present-centred experience during mindfulness practice may lead to a weighing of incoming sensory information over prior information during the perceptual process. This interpretation hence raises the intriguing possibility that mindfulness may mitigate the well-documented biasing influence of prior expectations and information on pain perception. We tested this hypothesis across three separate pain expectancy-manipulation paradigms.

Study 1 investigated whether the instructed use of a mindfulness strategy vs. an vsernative cognitive regulatory strategy (i.e., suppression) differentially modulates susceptibility to conditioned hypoalgesic and hyperalgesic effects during an implicit classical pain conditioning paradigm. The results revealed that while participants assigned to the suppression condition exhibited preserved cue-induced hypoalgesic effects, no such effects were observed for the mindfulness condition.

In Study 2, we employed a recently developed pain categorization paradigm to test whether trait mindfulness level modulates the influence of prior categorical information on pain perception and pain-related decision-making. Although the paradigm successfully elicited categorization-induced perceptual biases, modulation of these effects did not differ across individuals with high and low trait mindfulness.

Finally, in Study 3, we used an explicit pain-cueing paradigm in which we aimed to address some of the methodological limitations of Study 1. The analyses revealed that high trait mindfulness scorers reported smaller cue-induced hyperalgesic effects for pain unpleasantness ratings compared to low trait mindfulness scorers. There were, however, no group differences in cue-induced hypoalgesia.

Results from the pain conditioning studies provide partial support for the notion that mindfulness may mitigate the influence of prior expectations and information on pain perception. These findings add to growing evidence suggesting that mindfulness may alleviate pain via neuropsychological mechanisms opposite to those typically involved in conditioning/placebo-induced hypoalgesia. The discussion section explores potential methodological and mechanistic explanations for the asymmetric pattern of results observed across the three studies and considers the potential clinical implications of those findings.

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1 Introduction

Over the past few decades, mindfulness has risen from the fringes of scientific curiosity to permeating major aspects of contemporary society, including public healthcare, education and the criminal justice system. Paralleling and arguably promoting its soaring popularity in the public eye has been the exponential rise in scientific publications documenting the therapeutic and cognitive effects of mindfulness practice (Chiesa et al., 2017). Yet, in spite of this burgeoning empirical interest, several important questions remain unanswered: most notably, the question of why and how mindfulness practice conveys its purported effects.

1.1 Mindfulness: From conceptualisation to operationalisation

The concept of mindfulness traces its roots back to the Pali term *Sati*, which scholarly accounts of early Buddhist scriptures have interpreted to connote lucid awareness of what is occurring within the phenomenological field (Bodhi, 2011) or bare attention (Thera, 1986). Building on these traditional descriptions, Kabat-Zinn (1994, p. 4) coined the commonly cited definition of mindfulness as “paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally”. Although aiming to provide an intuitive introduction to the construct of mindfulness, these early definitions do not lend themselves easily to operationalization within the experimental context. In a consensus paper, Bishop et al. (2004, p. 234) aimed to offer such an operational definition of mindfulness as “a process of regulating attention in order to bring a quality of non-elaborative awareness to current experience and a quality of relating to one’s experience within an orientation of curiosity, experiential openness, and acceptance”. Similar attempts have since followed, including definitions of mindfulness as “awareness, of present experience, with acceptance” (Germer, 2005, p.7) “as a state of consciousness in which attention is focused on present moment phenomena occurring both externally and internally” (Dane 2011, p. 1000), “a bare and continuous moment-to-moment awareness of our experience” (Schmidt, 2004, p. 9), “a receptive attention to and awareness of present-moment events and experience” (Brown et al., 2007, p .212) and “a psychological construct associated with nonjudgmental attention and awareness of present-moment experiences” (Long & Christian, 2015). Although it is clear from this plethora of offered definitions that a clear consensus is still lacking, these definitions nevertheless share some common core features, namely the continuous moment-to-moment monitoring of arising physical and mental phenomena, coupled with an attitude characterised by non-judgment and acceptance. As such, while much work still needs to be done on a consensual definition of mindfulness and without intending to diminish the importance of such an endeavour (see Van Dam et al. (2018) for a relevant critique of the potential implications of the current semantic ambiguity surrounding mindfulness), I would preface this thesis by emphasising that mindfulness-related evidence presented throughout this manuscript will be predominantly described and discussed along the lines of these core components.

1.2 Disentangling the underlying mechanisms of mindfulness through the lens of pain perception

Although often thought of as a singular construct, pain is a complex and continually changing subjective experience which is constructed and modulated by a myriad of sensory, cognitive and affective factors (e.g., location, duration, intensity, expectations, beliefs, anxiety, mood etc.). As such, pain is commonly conceptualised as consisting of both a sensory-discriminative dimension and an affective-motivational dimension (Price, 2000; Auvray et al., 2010). This bi-dimensionality is also evident in the International Association for the Study of Pain (IASP)'s recently revised definition of pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (Raja et al., 2020). Accordingly, the subjective experience of pain is commonly assessed within the experimental setting using both pain intensity (targeting the sensory-discriminative component) and pain unpleasantness (targeting the affective-motivational component) self-report measures. This distinction is also notably highlighted in an early Buddhist scripture, the *Sallatha Sutta* (translated as The Arrow; Ṭhānissaro Bhikkhu, 1997), which posits that mindfulness practice helps in fully experiencing the sensory aspect of pain (referred to as the first arrow of pain) while also letting go of its evaluative component (the second arrow of pain). Pain perception thus offers a valuable pathway for investigating this potential uncoupling of sensory and affective dimensions.

Moreover, both pain perception and its modulation by mindfulness practice have garnered considerable scientific interest within the neuroscientific community. This rise in brain imaging investigations of mindfulness-induced hypoalgesia has resulted in novel evidence suggesting that mindfulness may involve unique neural mechanisms compared to other forms of cognitive pain modulation strategy (as will be reviewed further below). These new insights thus provide an interesting theoretical foundation for the formulation of neurophysiologically-informed mechanistic accounts of mindfulness.

Finally, and of utmost relevance to the thesis, experimental pain paradigms allow the investigation of pain perception in light of unexpected or contradictory pain-related information. The influence of prior beliefs and information on pain perception at both the behavioural and neural levels has been vastly documented across a series of pain expectancy-manipulation paradigms (Atlas & Wager, 2012). As will be discussed further below, modulating the relationship between expected sensation and actual sensory input is of paramount importance to testing our proposed mechanistic model. In a similar vein, experimentally-induced pain stimuli offer the researcher increased experimental control over the intensity of the (nociceptive) sensory input, compared to stimuli that are typically used in other affective domains (e.g., anxiety or mood modulation studies). For instance, the experimenter can manipulate pain intensity by increasing or decreasing the temperature of a painful heat stimulus (with the underlying assumption being that higher temperatures should result in higher intensity reports), and, if desired, adjust stimuli temperatures individually for each participant in accordance with their pain tolerance levels.

1.3 Mindfulness and pain modulation: A brief literature overview

Predictably, the effects of mindfulness-based interventions on pain experience and pain symptomology have been the subject of considerable empirical interest. However, a clear and definite synthesis of the relationship between mindfulness and pain is made difficult by the fact that these effects have often been investigated using various forms of mindfulness-based interventions in varying participant samples and with a variety of outcome measures. Nevertheless, a meta-analytic approach can help in accounting for these inter-study differences and in providing a cohesive overall picture of the current status of mindfulness-driven pain modulation research. The following paragraph provides an overview of published meta-analytic evidence pertaining to the effects of mindfulness on various pain-related outcomes.

In an early meta-analytic study on the treatment of somatization disorders, Lakhan and Schofield (2013) found a small to moderate positive effect of mindfulness-based therapies on pain (Standardized Mean Differences (SMD:−0.21) and symptom severity (SMD: −0.40) reductions. Likewise, Lauche et al. (2013) reported short-term improvements in pain reports in patients with Fibromyalgia syndrome following mindfulness-based stress reduction (MBSR) interventions, relative to usual care (SMD: −0.23) and active control interventions (SMD: −0.44), although they failed to find any significant long-term differences. In a comprehensive meta-analytic review of the clinical effects of acceptance- and mindfulness-based interventions on chronic pain, Veehof et al. (2016) found significant reductions in pain intensity (SMD: −0.24) and pain interference (SMD: −0.51). A similar study by Bawa et al. (2015) also demonstrated improved perceived pain control (SMD: 0.58) following mindfulness-based interventions. Focusing specifically on patients with low back pain, Anheyer (2017) revealed that MBSR interventions induced reductions in pain intensity (SMD: −0.48), relative to usual care but not to other active comparators. Zou et al. (2018) reported that a specific mindfulness-based exercise (i.e., Baduanjin) was largely successful at alleviating musculoskeletal pain (SMD: -0.88), while Gu et al. (2018) found significant mindfulness meditation-induced improvements in primary headache pain intensity (SMD: -0.89) and frequency (SMD: -0.67). Zou et al. (2019) also reported favourable effects of mindfulness exercises on pain intensity reports in chronic low back pain patients (SMD: -0.37). Khoo et al. (2019) revealed significant reductions in pain intensity reports following MBSR interventions for chronic pain treatment relative to control interventions (SMD: -0.34), but not relative to cognitive-behavioural therapies. In contrast, Pei et al. (2020) observed short-term improvements on depression mood (SMD: -0.72) but not in pain intensity, pain interference and pain acceptance following Mindfulness-based Cognitive Therapies (MBCT) relative to non-MBCT interventions. Finally, Shires et al. (2020) recently investigated the effects of mindfulness-based interventions on acute pain and found beneficial effects of mindfulness on pain tolerance (SMD: 0.68) and pain threshold (SMD: 0.72), but not on pain severity or pain-related distress.

A clear take-out from this meta-analytic literature overview is that the magnitude of mindfulness-driven hypoalgesic effect sizes is still the subject of much debate. As hinted to previously, this variance in effect sizes could be attributed to the differences in the form and duration of mindfulness intervention used, participant samples (healthy vs patient population), pain symptomology and pain outcome measures employed across studies. Nonetheless, the overall meta-analytic picture does lend support to the notion that mindfulness-based interventions may hold promising pain-alleviating potential. A key remaining question however is how mindfulness practice actually conveys these benefits. Our understanding of the mechanisms of mindfulness has so far lagged significantly behind the clinical validation of its effects. Nevertheless, recent insights from neuroimaging studies of mindfulness-induced pain modulation may provide a promising avenue for addressing this question.

1.4 Neural underpinnings of pain perception and its modulation

In order to grasp an accurate picture of the neuropsychological mechanisms involved in mindfulness-induced pain modulation, it is first important to outline the neural underpinnings of pain perception and its cognitive modulation. As highlighted above, pain is a complex dynamic subjective experience that comprises sensory, affective, motivational and cognitive components. This complexity is reflected in the widely distributed and multidimensional neural circuitry involved in the transmission and integration of nociceptive information (Garland, 2013; Khalid & Tubbs, 2017). In neurophysiological terms, the process of pain perception has been traditionally represented as arising from the initial registration of nociceptive sensory inputs at primary peripheral afferents associated with the location of (actual or potential) tissue damage, and their subsequent transduction along the myelinated (fast-pain) A-delta fibers and unmyelinated (slow-pain) C-fibers to the dorsal horn of the spinal cord. From there, the nociceptive information ascends up the spinothalamic tract to the thalamus, which serves as the primary ‘relay station’ for sensory information to the subcortical and cortical areas. The nociceptive information is initially relayed from the different subdivisions of the thalamic nuclei to lower-level sensory processing regions, including the periaqueductal grey, amygdala, primary and secondary somatosensory cortices and basal ganglia. The sensory information is then transmitted to the insular regions and the anterior cingulate cortex, which are believed to play key roles in salience detection, self-awareness, interoception, allocation and monitoring of attention, and anticipation. Finally, the nociceptive information is believed to be ascribed contextual, affective and motivational value through activation of higher-order prefrontal cortices.

This description, however, depicts the shaping of pain experience as a predominantly bottom-up driven process, with nociceptive information ascending from low-level afferents, through the cortical hierarchy, until their eventual interpretation by higher-order level neural processes. Yet, perceptual pain experience is also highly dependent on the context within which it arises. The empirical pain literature is rife with evidence showing that factors such as prior beliefs, pain-related fear or catastrophizing, coping strategy used, desires, anxiety, previous experiences, habituation, sensitization etc. can all dramatically attenuate or amplify the subjective experience of pain (Atlas and Wager, 2012; Villemure and Bushnell, 2002; Wiech et al., 2008; Wiech, 2016; Zeidan and Vago, 2017). At the neural level, increases in experienced pain reports have been linked with activation of several of the brain regions mentioned above, including the primary and secondary somatosensory cortices, thalamus, anterior cingulate cortex, and the anterior and posterior insula (Apkarian et al., 2005; Coghill et al., 2003; Derbyshire et al., 1997; May, 2007; Porro et al., 1998).

Conversely, these brain regions have been shown to exhibit reduced activity when pain was modulated top-down via cognitive forms of pain regulatory strategies. Cognitive pain modulation strategies include distraction from pain (attentional diversion), cognitive reappraisal, hypnosis, and placebo analgesia. For example, a series of studies on distraction from pain have reported reduced activity in the somatosensory cortices, insula, thalamus, and midcingulate cortex (Bantick et al., 2002; Petrovic et al., 2000, Seminowicz et al., 2004). Similarly, placebo hypoalgesia has been associated with reduced activity in the anterior cingulate cortex (ACC), insula and thalamus (Bingel et al., 2006; Petrovic et al., 2002; van der Meulen et al., 2017; Wager et al., 2004; Wiech et al.,2008), while perceived control over pain has been associated with reductions in activity in the ACC, insula, and secondary somatosensory cortex (Salomons et al., 2004; Wiech et al., 2008). Although the different forms of cognitive pain modulation likely operate along different mechanisms (Buhle et al., 2012), there is converging evidence that neural mechanisms that are typically involved in the top-down modulation of pain include regions pertaining to the frontoparietal network (i.e., the prefrontal and parietal cortex) as well as the (rostral) anterior cingulate cortex (ACC), and descending pain control systems, such as the periaqueductal grey (PAG) (Eippert et al., 2009; Knudsen et al., 2011; Kong et al., 2013; Kupers et al., 2005; van der Meulen et al., 2017). These cognitive regulatory strategies provide a useful backbone against which to compare, and potentially identify, unique neural mechanisms involved in mindfulness-related pain modulation.

1.5 Neural underpinnings of mindfulness-related pain modulation

In an early fMRI study, Grant et al. (2011) reported that a group of Zen practitioners, with extensive meditative practice, exhibited higher pain thresholds (i.e., they required higher thermal heat temperatures to elicit moderate pain levels) compared to demographically matched non-meditators. Interestingly, the meditators showed reduced neural activity in areas typically associated with affective and memory-related processing (prefrontal cortex, amygdala, hippocampus) but elevated neural activity in several nociceptive processing areas (anterior cingulate cortex, thalamus, insula) during pain stimulation, relative to the non-meditators. Crucially, they also found that greater decoupling between the executive and pain-related regions were predictive of higher pain tolerance in the meditators group. Gard et al. (2012) conducted a similar study whereby long-term mindfulness practitioners and matched non-meditators were administered noxious electric stimuli while they engaged in mindfulness practice or a no-instructions control condition. Mindfulness practitioners, but not controls, reported lower anticipatory anxiety and pain unpleasantness (but not pain intensity) ratings during the mindful condition. In line with Grant et al.'s findings, this mindfulness-induced pain relief was associated with increased activation of the right posterior insular and secondary sensorimotor cortex, and reduced activation of the lateral prefrontal cortex. Focusing on open presence forms of meditation, Lutz et al. (2013) also found that expert meditators reported lower pain unpleasantness, but not pain intensity, ratings compared to novice meditators. This group difference was linked to increased activation of the dorsal anterior insula and anterior mid-cingulate during pain for the expert meditators. Interestingly, the expert group also exhibited lower activity in these areas and the amygdala during the pre-stimulus anticipatory phase. Two recent studies instead looked at the neural mechanisms underlying the relationship between trait/dispositional mindfulness levels and pain sensitivity. Harrison et al. (2019) found a positive association between higher trait mindfulness level and pain tolerance. Higher trait mindfulness was also associated with weaker connectivity between the central nodes of the default mode network (typically associated with self-referential processing) and stronger connectivity between the precuneus and the somatosensory cortices. Zeidan et al. (2018) reported that trait mindfulness was linked to lower pain intensity and unpleasantness ratings. Higher trait mindfulness was again linked to reduced activation of brain networks linked to self-referential processes. Neuroimaging studies of brief mindfulness training have, however, revealed slightly different activation patterns. Across two studies, Zeidan et al. (2011; 2015) found that novice meditators reported lower pain intensity and unpleasantness ratings after undergoing brief mindfulness training. Mindfulness-induced reductions in pain ratings were associated with increased activation of the right anterior insula, anterior cingulate cortex and orbitofrontal cortex, and with reduced thalamic activity.

Overall, these findings suggest that mindfulness-driven pain alleviation may involve unique neural mechanisms, characterised by enhanced sensory-discriminatory processing of painful stimuli and the abatement of memory-based and cognitive-evaluative processes. Given the well-documented positive association between increased activation of pain-related sensory processing areas and amplified pain reports, this neural pattern may seem highly counter-intuitive. These findings are however very much in line with aforementioned conceptualizations of mindfulness as a non-judgmental and non-elaborative (i.e., curtailed cognitive-evaluative activation) form of sustained attention directed at present-moment phenomena (i.e., increased sensory processing activity). The following sections explore how recently formulated predictive processing models of perception may offer particularly promising unificatory potential for the integration of these novel neuroimaging insights and traditional accounts of mindfulness practice, and the testable hypotheses that can be derived from them.

1.6 Predictive processing: A primer

At the heart of the predictive processing framework is the premise that the brain serves the core biological imperative of maintaining homeostasis in the face of a constantly changing environment, i.e., its fundamental function is to minimize the likelihood of incurring surprising encounters and physiological states that fall outside the conditions necessary for the organism's survival (Friston, 2009). To do so, the brain constructs, maintains and continuously updates an internal model of its (exteroceptive as well as interoceptive) environment, based on its homeostatic needs and past interactions with said environment.

Predictive processing models (sometimes also referred to as predictive coding or the free-energy minimization principle in its most comprehensive articulation) completely overturn the classical treatise of the brain as a mere "stimulus-response" organ, whereby perception (and neural activity along the cortical hierarchy) is driven in purely "bottom-up" fashion by sensory inputs from the external world. Instead, the brain is formalised as an active inferential machine which constantly anticipates and instantiates predictions about upcoming sensory states, based on a constructed internal model of the causal statistical regularities of its environment (Clark, 2013).

Central to the predictive processing framework therefore are the continuous comparisons between, and integration of, predicted and observed sensory states. This ongoing inferential process can be described along the following iterative sequence: *(i)* a priori predictions about upcoming sensory signals are derived from the internal (generative) model; *(ii)* the predicted sensory signal is compared with the actual sensory signal; and (iii) any discrepancy between the predicted and observed sensory data (i.e. prediction error) is propagated upstream along the cortical hierarchy and minimized by being either acted upon or via a revision of the model (Friston, 2010). This iterative matching of prediction with inputs occurs at every level of the cortical hierarchy with each level predicting the sensory activity at the level below it, thus effectively explaining away incoming information consistent with the prediction, with only the unexplained portion of the sensory input ascending to higher levels of the neural hierarchy.

Computationally, this theoretical framework is deeply ingrained in Bayesian principles. In cognitive terms, the Bayesian view of perception can be understood as describing how prior beliefs, expectations or information about future sensory events are integrated with newly observed sensory information, resulting ultimately in an updated posterior belief (i.e., the actual percept). Importantly, to reflect the inevitable uncertainty, ambiguity and noise associated with a priori predictions and the sensorium (i.e., the predictable unpredictability of the world), both prior beliefs and ascending prediction errors are characterised as probability distributions, i.e., with a location (mean) and a precision (i.e., inverse variance) estimate. Precision in this context can be thought of as the level of confidence assigned to the prior expectation, or the extent to which the ascending sensory prediction error can be trusted (i.e., signal-to-noise ratio). Crucially, for our purposes, these precision estimates are deployed via the process of attention allocation (Feldman & Friston, 2010). In other words, attending to a particular sensory stream ascribes, and maintains, an expectation of enhanced precision to that ascending prediction error (implemented at the neural level via modulation of the corresponding post-synaptic gain). Attention allocation therefore plays a critical role in determining how prediction errors are minimised, and thus on the resulting percept.

According to the predictive processing framework, discrepancies between predicted and actual sensory data (i.e., prediction errors) can be minimised in two ways: either (i) by actively seeking sensory stimulation that best fit the prediction or (ii) by updating the internal model to best accommodate the incoming sensory data. The first mode is typically referred to as active inference. In active inference, the prior prediction generated from the internal model is afforded higher weight (precision) relative to the ascending prediction error, and thus promotes responses intended to bring the sensory signal in line with the expected state. It must be noted that active inference does not necessarily entail overt behavioural responses, i.e., these processes can take place at a purely physiological, autonomic regulatory level (Gu and Fitzgerald, 2014). Nonetheless, when faced with stressors of a particularly aversive or threatening nature (e.g., painful sensations) and which exceeds one’s autonomic regulatory capacity, prediction errors may ascend to higher levels of the cortical hierarchy prior to resolution. Minimisation of such prediction errors would then necessitate overt behavioural interactions with the environment in order to reach the expected state. As such, cognitive pain regulatory strategies such as suppression, distraction and re-appraisal can all be subsumed under the active inference modality, as they involve overt attempts at altering the characteristics of the nociceptive signal in order to bring it in line with the expected or desired state.

Predictive processing models of mindfulness however posit that mindfulness may instead be an example of the second mode of prediction error minimisation, i.e., perceptual inference. In perceptual inference, higher weight (precision) is assigned to the actual sensory input (i.e., deemed more reliable) relative to the predicted state. Perceptual inference thus encourages the revision and updating of prior beliefs embedded in the internal model rather than prompting efforts to restore prior states. This process hence entails a posterior distribution (i.e., conscious percept) that is more closely aligned to the actual sensory input. The following section describes how the core tenets of mindfulness practice may fit under this perceptual inference modality.

1.7 The praxis of mindfulness meditation from a predictive processing perspective

Before framing mindfulness within a predictive processing context, it is important to first outline the core features of mindfulness meditative practice. Although not a prerequisite for the development of mindfulness, mindfulness meditation is the most commonly used technique to train and evoke a state of mindfulness. Although several forms of meditative practices can be subsumed under the umbrella term “mindfulness meditation”, these nevertheless do share some core essential steps. At the beginning of a meditative session, the practitioner typically adopts a comfortable but stable upright posture. Focus of attention is then deliberately oriented and sustained on a specific target (e.g., localised breathing sensation). Whenever attention drifts away from the object of focus to a distractor sensory, affective or cognitive event, the practitioner is instructed to kindly acknowledge the distractor without any emotional or analytical engagement with the discursive event, and to redirect attention back to the meditative target. This continuous focusing and re-focusing of attention help to enhance attentional stability. Over time, the increased attentional stability eventually dampens the tendency to reflexively engage with arising sensations, thoughts or feelings. Phenomenologically, this is often experienced as a transition from a state of focused attention to a state of open monitoring awareness, whereby the practitioner gradually develops the ability to effortlessly monitor ongoing experience without the urge for emotional reactivity or cognitive elaboration. This state has also been described as one of decentering or meta-awareness.

Several authors have recently attempted to formalise these core components of mindfulness practice in predictive processing terms (Farb et al., 2015; Lutz et al., 2019; Manjaly & Iglesias, 2020; Pagnoni, 2019). As highlighted previously, within the predictive processing context, attention allocation is the process by which ascending sensory prediction errors are afforded their precision estimate and thus their influence on the perceptual process, relative to prior expectations. One of the key prescriptions of meditative practice is the sustained attention towards the ongoing influx of physical and mental phenomena. In predictive processing terms, this heightened sustained attention should drive an increase in the precision of ascending sensory information (in line with the increased sensory processing neural activity observed during mindfulness practice). Likewise, these authors suggest that immobility of posture and gaze encouraged in meditative is not arbitrary but instead serves to further enhance the signal-to-noise ratio of proprioceptive and interoceptive signals. Conversely, the re-orienting of attention away from habitually activated mental content (as in episodes of mind-wandering) and back to the non-elaborative monitoring of current experience has been hypothesised to lead to a down-weighting of the influence of cognitive and emotional expectations/desires (as reflected in the reduced activation of evaluative and memory-related neural processes). Altogether, these processes may combine so that afferent sensory information may be prioritized over a priori expectations during the perceptual process. These models hence raise the intriguing possibility that mindfulness may promote perceptual objectivity, i.e., mindful awareness may mitigate the influence of prior expectations and beliefs on perceptual experience. However, this interpretation has so far relied largely on reverse inferencing and has yet to be submitted to extensive empirical testing. In the next section, I put forward the argument that pain expectancy-manipulation paradigms may provide an ideal testing ground for this hypothesis.

1.8 Pain expectancy manipulation as ideal testing ground

As highlighted previously, the empirical pain literature is rife with evidence documenting the biasing influence of prior beliefs, expectations, and information on pain experience (Atlas & Wager, 2012). Accordingly, the neural mechanisms underlying expectancy-driven biases have been the subject of considerable interest within the pain research community. Of particular note are a series of recent neuroimaging studies suggesting that mindfulness-induced pain relief may involve contrasting neural patterns to those observed in placebo analgesia (Case et al., 2021; Wells et al., 2020; Zeidan et al., 2015, Zeidan et al., 2016).

Furthermore, numerous predictive processing accounts explicating the role of expectations on pain experience, in terms of heightened precision of priors, have been formulated in recent years (Büchel et al., 2014; Hechler et al., 2016; Ongaro & Kaptchuk, 2019; Tabor et al., 2017). Accordingly, an increasing number of studies have suggested that the effects of expectation on pain perception fit particularly well with specific predictions derived from the predictive processing framework. For instance, Brown et al. (2008) and Colloca et al. (2010) have previously demonstrated that more precise expectations tend to amplify the effects of expectations on pain. Furthermore, computational modelling investigations of expectancy-driven pain modulation have shown that Bayesian models of perception (akin to the ones postulated within predictive processing frameworks) tend to outperform other models for both behavioural (Anchisi and Zanon, 2015, Jung et al., 2017; Hoskin et al., 2019) and neural outcomes (Geuter et al., 2017; Grahl et al., 2018).

As such, given its reliance on prior expectation and information, expectancy-driven pain modulation provides a particularly promising avenue for exploring the potential mechanisms of mindfulness. As predictive processing accounts suggest that mindfulness may weigh incoming sensory information over prior expectations, we may expect to observe reduced susceptibility to expectancy-induced pain perceptual bias during mindfulness practice and in highly mindful individuals.

1.9 Research aims and methodology

The overall aim of the project was to investigate the core claim from aforementioned predictive processing accounts suggesting that mindfulness may mitigate the influence of prior expectations and information on perception. We tested this hypothesis across three separate pain expectancy-manipulation paradigms.

In Study 1, we tested whether the instructed use of a mindfulness strategy vs. a contrasting cognitive regulatory strategy (i.e., suppression) during experimentally induced pain differentially modulates conditioned hypoalgesia and conditioned hyperalgesia, using a classical implicit pain-cueing paradigm. Given the contrasting neural activation patterns observed across mindfulness and other forms of top-down pain regulatory strategies, we hypothesised that participants assigned to the mindfulness would report reduced conditioned hypoalgesic and hyperalgesic effects, relative to the suppression group.

In Study 2, we employed a recently developed pain categorization paradigm (van der Meulen et al., 2017) to test whether trait mindfulness level modulates the influence of prior categorical information on pain perception and pain-related decision-making. In their study, van der Meulen et al. showed that arbitrarily assigning pain stimuli to specific categories can lead to increased perceived similarity for stimuli attributed to the same category (assimilation effect) and reduced perceived similarity for stimuli attributed to separate categories (accentuation effect). Given the novelty of the paradigm, we first aimed to replicate these findings using a slightly modified version of the paradigm (Study 2(a)). We then conducted a second separate study (Study 2(b)), in which we tested whether individuals with high trait mindfulness levels show reduced susceptibility to categorization-induced biases in pain perception and decision-making, compared to low trait mindfulness individuals.

In Study 3, we used an explicit pain-cueing paradigm in which we aimed to address some of the methodological limitations of Study 1. The study comprised the same sample of participants as Study 2(b). We again hypothesised that highly mindful individuals would report reduced conditioned hypoalgesic and hyperalgesic effects, relative to low trait mindfulness individuals.

1.10 References

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2 STUDY I: Brief Mindfulness Training Can Mitigate the Influence of Priors on Pain Perception

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2.1 Abstract

Recent neuroimaging evidence suggests that mindfulness practice may mitigate the biasing influence of prior cognitive and emotional expectations on pain perception. The current study tested this hypothesis using a pain-cueing paradigm, which has reliably been shown to elicit conditioned hypoalgesic and hyperalgesic effects. Specifically, we aimed to investigate whether the instructed use of a mindfulness compared to a suppression strategy differentially modulates the magnitudes of conditioned hypoalgesia and hyperalgesia. Sixty-two healthy non-meditators were assigned to listen to either brief mindfulness or suppression instructions, in between the conditioning and testing phases of a pain-cueing task. Participants provided ratings of anticipatory anxiety, pain intensity and pain unpleasantness throughout the task. They also completed trait and state self-report measures of mindfulness and pain catastrophizing. Results indicated that the paradigm was successful in inducing conditioned hyperalgesic and hypoalgesic effects. Importantly, while we found evidence of cue-induced hyperalgesia in both groups, only the suppression group reported cue-induced hypoalgesia. No group differences in pain ratings were found for unconditioned (novel-cued) stimuli. These findings provide partial support for recently proposed predictive processing models, which posit that mindfulness may lead to a prioritization of current sensory information over previous expectations. We explore potential explanations for the asymmetrical group differences in conditioned hypoalgesia versus conditioned hyperalgesia, and discuss our results in light of recent neuroimaging insights into the neuropsychological mechanisms of mindfulness and expectancy-driven pain modulation.

2.2 Introduction

An extensive body of literature has linked mindfulness-based interventions to increased pain tolerance, lower pain unpleasantness and improved pain symptomology across a wide range of chronic pain conditions (Hilton et al., 2016; Lakhan & Schofield, 2013; Veehof et al., 2011; 2016). Yet, despite this surge of interest in its clinical effects, little is known as to how mindfulness conveys these benefits.

Successful cognitive modulation of pain (e.g., via distraction, suppression, placebo and reappraisal) is typically accompanied by reduced activation of brain regions commonly associated with pain processing (Atlas & Wager, 2012; Jensen et al., 2016; Knudsen et al., 2011). Recent neuroimaging evidence, however, suggests that mindfulness-driven pain relief may instead elicit a contrasting neural pattern, involving increased activation of areas associated with the sensory-discriminatory processing of painful stimuli and reduced activation of putatively cognitive-evaluative regions (Gard et al., 2011; Grant et al., 2011; Lutz et al., 2013; Zeidan et al., 2011; Zeidan et al., 2015). While these findings may appear counter-intuitive, they are nevertheless in line with traditional conceptualisations of mindfulness as a non-judgmental, non-elaborative and non-conceptual (i.e., abatement of evaluative and memory-related processes) form of awareness towards the ongoing flux of present moment experience (i.e., enhanced sensory processing activity). In light of these observations, recently formulated predictive processing accounts posit that mindfulness may, via the reallocation of attention to current experience, lead to an amplification of afferent sensory signals and a concomitant attenuation of the relative weight ascribed to a priori expectations (Farb et al., 2015; Pagnoni & Porro, 2014). This assumption raises the possibility that mindfulness may reduce susceptibility to the well-documented biasing influence of prior cognitive and emotional expectations on pain experience (Atlas & Wager, 2012). While this interpretation has so far relied largely on reverse referencing, preliminary evidence from Taylor et al. (2018), showing that experienced meditators exhibit reduced hyperalgesic effects relative to controls following a fear conditioning procedure, provides initial support for this notion. Given the same overarching hypothesis that mindfulness mitigates the influence of priors on perception, we would expect to find similar evidence for mindfulness-induced reductions in conditioned hypoalgesia. Moreover, how these modulatory effects of mindfulness compare with other top-down regulatory strategies remains an open question.

In the current study, we used a classical pain-cueing paradigm to assess whether the instructed use of a mindfulness or a suppression strategy differentially modulates conditioned hypoalgesia and hyperalgesia. Contrary to mindfulness, suppression strategies encourage the inhibition, rather than acceptance, of unwanted emotional and physical experience. Pain-cueing paradigms provide an ideal testing ground for the current hypothesis, given the elicited mismatch between incoming sensory information and conditioned expectations. Previous research has shown that heat stimuli of equivalent temperature are rated as more painful if preceded by a conditioned high-pain cue and less painful if preceded by a conditioned low-pain cue (Madden et al., 2015). We hypothesised that participants assigned to the mindfulness condition would report reduced cue-induced hypoalgesia and hyperalgesia, relative to the suppression group.

2.3 Methods

2.3.1 Design

The study used a 3x2 mixed factorial design, with Cue Type (low vs. novel vs. high pain cues) as the within-subject factor and Group (mindfulness vs. suppression) as the between-subject factor. The dependent variables consisted of self-reported anticipatory anxiety, pain intensity and pain unpleasantness ratings.

2.3.2 Participants

Participants were recruited via flyers and the University's webpage for study opportunities. Participants were invited to take part in a study investigating the psychological processes behind the coping strategies people commonly use when dealing with pain and anxiety. The flyers did not include any mention of conditioning, expectancy manipulation, mindfulness or suppression in order to rule out potential placebo or demand effects unrelated to our experimental manipulation. Ninety-two individuals initially expressed interest in the study. A screening procedure was conducted prior to the study to ensure that participants did not have any acute or chronic pain, skin conditions, mental disorders or neurological diagnoses (anxiety, depression, post-traumatic stress disorder, schizophrenia, substance abuse, dementia, epilepsy, stroke or Parkinson's), and were not taking any medication with potential hypo/hyper-algesic effects. Sixty-eight healthy volunteers (50% female), with a mean age of 26.85 (SD = 7.35) met the inclusion criteria to take part in the study. None of the participants had prior experience with mindfulness practices. Participants provided written informed consent prior to participation and were remunerated via course credit or gift vouchers at the end of the session. The experiment was conducted in either English (N = 60), French (N = 3) or German (N = 5), according to the participant's preference. Questionnaires were also available in each language. The protocol was approved by the ethics committee of the University of Luxembourg (ref: ERP 17-036).

2.3.3 Pain-cueing paradigm

The pain-cueing task was divided into an acquisition (conditioning) and a testing phase. Two visual stimuli (a purple and a green fixation target) served as cues during the acquisition phase. The fixation targets were in the shape of a combined bullseye and cross hair (based on Thaler et al., 2013). One of the cues (high pain cue) was systematically followed by a high pain stimulus while the other (low pain cue) always preceded a low pain stimulus (see Figure 1(a)). Cue colour-stimulus pairings were counterbalanced across participants. The visual cue was initially presented for 4 seconds. The cue then disappeared from the screen and was followed by an anticipatory phase ranging between 4-6 seconds. The heat stimulus was then delivered for a duration of 12 seconds (see below). After each trial, participants indicated on VAS scales the levels of anticipatory anxiety (i.e., "how anxious were you prior to the stimulus"), "pain intensity" and "pain unpleasantness" they experienced during the trial (see VAS ratings section below). There was a 10-second interval between trials. The acquisition phase consisted of two blocks of eight trials each (i.e., 4 low pain-cued stimuli and 4 high pain-cued stimuli per block), with a self-timed break between each block. Presentation order of the low and high pain stimuli was randomised within each block.

The testing phase (see Figure 1(b)) consisted of three blocks of 12 test trials each and followed a trial timeline similar to the acquisition phase (see Figure 1(c)). The heat stimuli were preceded by either the low pain cue, the high pain cue or a novel unconditioned (brown) cue. In contrast to the acquisition phase, the stimulation temperature was identical across all 36 test trials (i.e., the medium pain intensity derived from the calibration procedure described below). Each testing block consisted of four stimuli of each condition (i.e., low cue, high cue and novel cue) presented in a randomised order. Six reminder trials (i.e., with the same cue-stimulus pairing as in the acquisition phase) were presented at the beginning of Block 1, to reduce any suspicion that the cue-stimulus relationship had been altered following the mindfulness/suppression induction. Four additional reminder trials were randomly interspersed within each of Block 2 and 3 to reduce the likelihood of premature extinction. There was an equal number of low-cued and high-cued reminder trials in each block.

2.3.4 Thermal pain stimulation

Heat stimuli were administered via a contact thermal stimulator (Somedic AB, Sweden), which was attached to the volar surface of the participant's left forearm. An individual pain calibration procedure was conducted prior to the pain cueing task. Participants received a pseudorandomised series of 20 heat stimuli (ranging from 43°C to 49.5°C) and were asked to indicate, via a mouse click, the level of pain experienced for each stimulus on a VAS scale (0 = 'No pain' to 100 = 'Unbearable pain'). An overall stimulus-response (i.e., temperature-VAS rating) curve was produced for each participant using a linear regression fitting process (Mischkowski et al., 2018), to derive individual temperatures that reliably elicit ratings of 40 (low pain), 60 (medium pain) and 80 (high pain). Heat stimulus delivery lasted 12 seconds (ramp up - 1.5 s, plateau - 9 s, ramp down - 1.5 s), with a baseline temperature of 35°C.

2.3.5 Pain coping instructions

We used a similar approach to that employed by Hooper et al. (2011) and Prins et al. (2014) for our mindfulness and suppression induction procedures. Participants were fitted with headphones and were randomly assigned to listen to a 10-minute audio recording of either mindfulness or suppression instructions, in-between the acquisition and testing phases of the pain-cueing paradigm. The instructions were adapted from scripts previously used by Garland et al. (2015). Participants, assigned to the mindfulness condition, were encouraged to "openly monitor any arising sensations, thoughts and emotions… in a non-judgmental, non-evaluative manner…. without seeking to modify, suppress or avoid them". For the suppression condition, participants were instructed to "focus on mentally blocking out any arising sensations, thoughts and emotions…and concealing any external manifestation of what (they) are currently experiencing". The experiential avoidance stance inherent to suppression provides a sharp contrast to the non-judgmental form of awareness encouraged by mindfulness, whilst allowing us to match both conditions in terms of instructions delivery format and length. All audio instructions were delivered by the same female narrator. The narrator was fluent in English, French and German. To encourage participants to make use of the audio instructions during the testing phase of the study, they were also provided with additional on-screen text instructions more directly applicable to the pain procedures (audio and text instructions in all languages are included as supporting information; AppendixS1). The text instructions were presented at the start of the testing phase. Participants were instructed to press the space bar once they finished reading the on-screen instructions. They were then presented with the following multiple choice comprehension check item: "During the next pain stimulation session, you should aim to ("A: accept" / "B: inhibit") incoming sensations, emotions and thoughts". The text instructions were repeated if the participant failed to respond correctly to the comprehension check.

2.3.6 Self-report measures

Five Facet Mindfulness Questionnaire

The Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006) was used to assess participants' dispositional mindfulness levels. The questionnaire comprises 39 items (e.g., "I watch my feelings without getting lost in them") tapping into five dimensions of mindfulness: observing, describing, acting with awareness, non-judging of inner experience and non-reactivity to inner experience. Each item is rated on a 1 (never or very rarely true) to 5 (always true) Likert scale with higher scores indicative of higher mindfulness levels. The items were averaged to compute a mean trait mindfulness score (Cronbach's α for the current sample =.83). Validated German (Michalak et al., 2016) and French (Heeren et al., 2011) adaptations of the FFMQ were also available.

Pain Catastrophizing Scale

The 13-item Pain Catastrophizing Scale (PCS; Sullivan et al., 1995) is a widely used pain measure, which assesses an individual's tendency to engage in catastrophic thinking about actual or anticipated pain. Items (e.g., "I worry all the time about whether the pain will end") are rated on a scale of 0 (not at all) to 4 (all the time). An overall pain catastrophizing score was computed, ranging from 0 to 52 (Cronbach's α = .89), with higher scores indicative of higher catastrophizing levels. Validated German (Meyer et al., 2008) and French (Sullivan et al., 1995) adaptations of the questionnaire were also made available to participants.

Toronto Mindfulness Scale

The Toronto Mindfulness Scale (TMS; Lau et al., 2006) was used to assess state mindfulness level. The 13-item questionnaire measures two factors, i.e., decentering (e.g., "I was aware of my thoughts and feelings without over-identifying with them") and curiosity (e.g., "I remained curious about the nature of each experience as it arose"). All items are rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much). A mean state mindfulness score (Cronbach's α = .80) was computed, as well as the decentering (Cronbach's α = .67) and curiosity (Cronbach's α = .85) subscale scores. Higher scores were indicative of higher state mindfulness levels. German and French adaptations of the questionnaire (translated and back-translated in line with recommended guidelines from the International Test Commission (2017)) were also devised specifically for the purpose of this study (see supporting information; AppendixS2).

Situational Pain Catastrophizing Scale

The Situational Pain Catastrophizing Scale (SCS; Campbell et al., 2010) is a 6-item adaptation of the PCS, which aims to capture catastrophizing cognitions during a specific experimental pain procedure on a 5-point Likert scale, with higher scores were indicative of higher catastrophizing levels. Items scores (e.g., "I thought that the pain might overwhelm me") were averaged to obtain a mean situational pain catastrophizing score (Cronbach's α = .82). Similar to the TMS, German and French adaptations were again devised for this study (using the trait French and German (trait) PCS as basis) (see supporting information; AppendixS3).

Anticipatory Anxiety and Pain (VAS) Ratings

Anticipatory anxiety (i.e., anxiety level of the participant before each pain stimulus), pain intensity (i.e., intensity of the pain stimulus) and pain unpleasantness (i.e., aversiveness of the pain stimulus) were assessed via visual analogue scales (VAS), ranging from 0 (not anxious/intense/unpleasant at all) to 100 (extremely anxious/intense/unpleasant). Furthermore, original instructions from Price et al. (1983) were used to clarify the distinction between pain intensity and pain unpleasantness to participants.

Manipulation Checks

A post-experiment multiple-choice manipulation check item was administered to assess whether participants successfully noticed the cue-stimulus contingency during the acquisition phase (see supporting information; AppendixS4). Participants also reported their level of confidence in their response on a Likert scale of 1 (not confident at all) to 5 (fully confident). In addition, participants were asked to rate (i) the clarity of the audio instructions, (ii) the extent to which they followed the instructions, (iii) how easy it was for them to follow the instructions and (iv) how successful they thought they were in applying the instructions, on a scale of 1 (not at all) to 7 (very much so).

2.3.7 Procedure

Upon arrival, participants provided written informed consent and completed the FFMQ and the PCS. Next, participants were tested in a laboratory room dedicated to experimentally induced pain research. Participants were seated in a reclining chair approximately 110 cm away from 24-inch screen monitor and used a lap desk fitted with a mouse and keyboard to respond to the VAS scales and manipulation check items. Participants first carried out the pain calibration procedure to derive individual temperatures for the low, medium and high pain stimuli. This was followed by the acquisition phase of the pain-cueing task. Once the acquisition procedure was completed, participants were randomly assigned (using an AB-BA block randomization procedure) to listen to either the mindfulness or the suppression audio recording and then underwent the testing phase of the pain-cueing paradigm. Participants filled in the TMS, the SCS and the manipulation checks questionnaire upon completion of the testing phase. Finally, they were fully debriefed as to the purpose of the study.

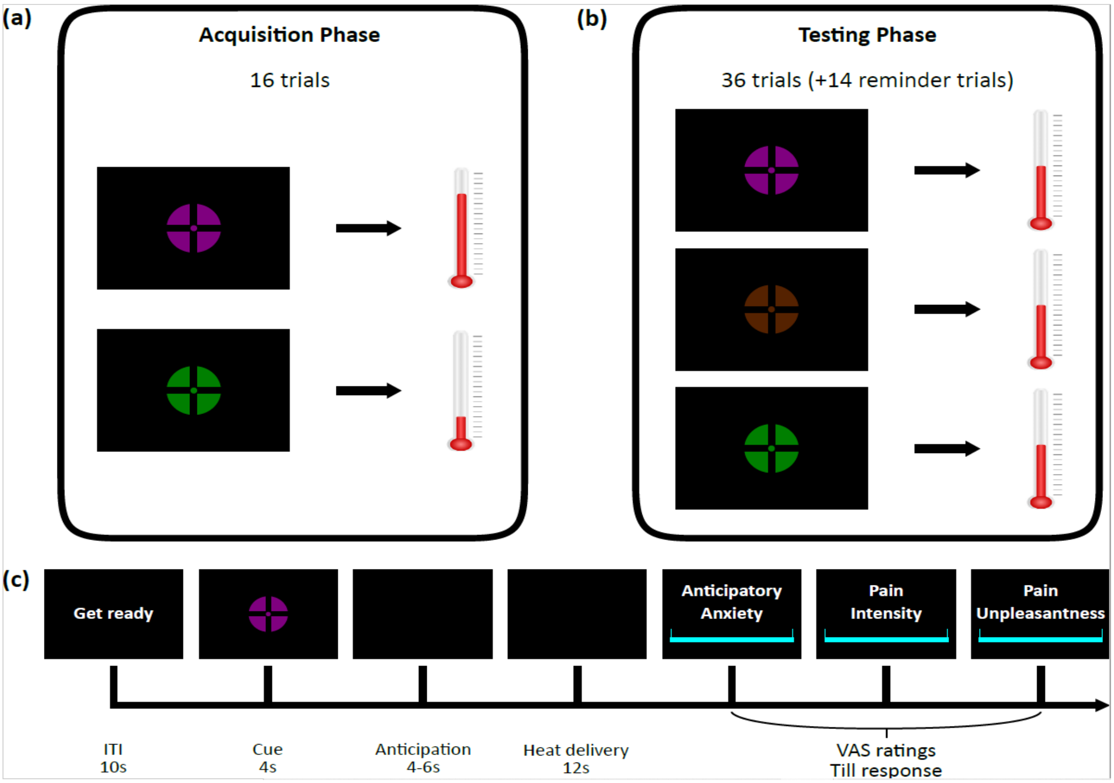


Figure 1 . Schematic representation of acquisition and testing blocks and trial timeline. (a) During the acquisition phase, one visual cue (e.g., purple) preceded the high pain stimuli while another cue (e.g., green) preceded the low pain stimuli (cue colour-stimuli contingency counterbalanced across participants). (b) During the testing phase, the high pain cue, the low pain cue and a novel cue (e.g., brown) were all followed by identical medium pain stimuli. (c) Depiction of the time-course for a typical trial.

2.3.8 Data analysis

Inspection of the manipulation check items revealed that six participants failed to correctly report the cue-stimulus contingency. As previous studies have reported evidence of conditioned hypoalgesia and hyperalgesia even in the absence of explicit awareness of the conditioning stimuli (Jensen et al., 2015), we conducted separate one-way repeated measures ANOVAs to determine whether Cue Type (low vs. novel vs. high) elicited different anticipatory anxiety, pain intensity and pain unpleasantness ratings, respectively. The analyses revealed no significant effect of Cue Type (i.e., conditioning effects) within this sub-sample of six participants (all p's $> .10$). As we were specifically interested in how the mindfulness and suppression conditions modulate the magnitudes of conditioned hypoalgesia and hyperalgesia, we excluded these six participants from the final analyses. Nevertheless, we would like to point out that supplementary analyses, including data from these six participants, showed a similar pattern of results to that reported in this manuscript. As a preliminary check, we also conducted independent t-tests to determine whether the language in which the study was conducted influenced the scores on the study items. The between-group comparisons showed no significant effect of language (all *p*'s > .10).

Next, we ran between-group multivariate GLM comparisons on the pre-experimental measures (FFMQ, PCS, temperature thresholds derived from the calibration procedure and pain ratings during the acquisition phase) to test whether our randomised participant allocation procedure was successful. We then ran similar analyses on the post-experimental measures (TMS, SCS and manipulation check items) to assess the effectiveness of our experimental manipulation.

To test our main hypotheses, we conducted separate two-way mixed ANOVAs, with Cue Type (low vs novel vs high) as the within-subjects factor and Group (mindfulness vs. suppression) as the between-subjects factor, for anticipatory anxiety, pain intensity and pain unpleasantness ratings, respectively. Greenhouse-Geisser corrections were applied wherever assumptions of sphericity were violated. Planned Bonferroni-adjusted ($p = .05/4$) follow-up pairwise comparisons were conducted to test whether ratings on novel-cued trials differed from low and high pain-cued trials respectively, across each group. Furthermore, we used a difference score approach to test whether the magnitudes of conditioned hypoalgesia and conditioned hyperalgesia differed between the mindfulness and suppression groups. Conditioned hypoalgesia (i.e., difference between novel-cued trials and low-cued trials) and conditioned hyperalgesia (i.e., difference between high-cued trials and novel-cued trials) magnitudes were computed for anticipatory anxiety, pain intensity and pain unpleasantness ratings separately. Individual two-way mixed ANOVAs, with Group (mindfulness vs suppression) as the between-subjects factor and Direction of modulation (conditioned hypoalgesia vs. conditioned hyperalgesia) as the within-subjects factor, were conducted for the anticipatory anxiety, pain intensity and pain unpleasantness ratings, respectively. We were specifically interested in any potential interaction effects, i.e., whether the two groups differed in terms of conditioned hypoalgesia and conditioned hyperalgesia magnitudes, respectively. Bonferroni-adjusted follow-up pairwise comparisons ($p = .05/2$) were again used to probe any significant interaction effects. Finally, we conducted exploratory (two-tailed Pearson) correlational analyses to test for potential associations between the self-report mindfulness and pain catastrophizing questionnaires (i.e., FFMQ, TMS, PCS and SCS) and cue-induced hypoalgesia and hyperalgesia.

2.4 Results

2.4.1 Baseline measures

The mindfulness (N = 31) and suppression (N = 31) groups did not differ in terms of gender distribution ($\chi^2(1, N = 62) = .07$, $p > .10$) or age ($t(60) = .33$, $p > .10$). Furthermore, no group differences in trait questionnaires scores or in temperature thresholds required to elicit low, medium and high pain during the calibration procedure were found. Finally, there were no group differences in anticipatory anxiety, pain intensity and pain unpleasantness ratings on low and high pain-cued trials during the acquisition phase, confirming that our randomisation procedure was successful. Table 1 summarizes the group means, SDs and statistics for the baseline measures.

Table 1. Mean (SD) and F values for baseline measures.

	Mindfulness (N = 31)	Suppression (N = 31)	F(1, 60)
FFMQ (1 - 5)	3.27 (0.27)	3.23 (0.40)	0.19
PCS (0 - 52)	20.55 (9.26)	19.26 (9.55)	0.29
Pain thresholds (°C)			
Low	45.63 (0.85)	45.24 (0.81)	3.33
Medium	46.63 (0.80)	46.29 (0.77)	2.77
High	47.65 (0.78)	47.32 (0.76)	2.84
Acquisition Phase			
Low-cued ratings (0 – 100)			
Anticipatory Anxiety	23.27 (11.60)	26.25 (15.52)	0.78
Pain Intensity	33.19 (10.54)	37.53 (11.36)	2.43
Pain Unpleasantness	30.55 (11.17)	32.46 (10.49)	0.48
High-cued ratings (0 – 100)			
Anticipatory Anxiety	40.56 (16.27)	48.40 (22.98)	2.41
Pain Intensity	80.33 (7.83)	81.20 (6.89)	0.21
Pain Unpleasantness	79.96 (7.82)	82.33 (7.55)	1.48
Pain Unpleasantness	79.96 (7.82)	82.33 (7.55)	1.48

FFMQ (Five Facet Mindfulness Questionnaire), PCS (Pain Catastrophizing Scale); scale ranges are provided alongside each measure.
Note: *** = p < .001, ** = p < .01, * = p < .05

2.4.2 State and manipulation check measures

Between-group multivariate GLM comparisons revealed that the two groups did not significantly differ in overall state mindfulness (TMS) scores, $F(1,60) = 2.43$, $p = .12$, $\eta_p^2 = .04$. However, when analysing the subscales, results indicated that the mindfulness group scored significantly higher than the suppression group on the decentering subscale, $F(1,60) = 7.88$, $p < .01$, $\eta_p^2 = .12$. No group differences were found for the curiosity subscale, $F(1,60) = 0.10$, $p = .92$, $\eta_p^2 = .00$. In addition, the mindfulness group reported marginally lower SCS scores than the suppression group, $F(1,60) = 2.89$, $p = .095$, $\eta_p^2 = .046$. Analyses of the manipulation check items indicated that the mindfulness group reported significantly greater confidence in their cue-stimulus contingency awareness response, $F(1,60) = 5.04$, $p = .03$, $\eta_p^2 = .08$. No group differences were observed for the other manipulation check items (p's all > .10). Table 2 summarizes the group means, SDs and statistics for the state and manipulation check measures.

Table 2. Mean (SD) and F values for state measures and post-experimental manipulation checks.

	Mindfulness (N = 31)	Suppression (N = 31)	F(1, 60)
SCS (0 – 4)	0.73 (0.57)	1.02 (0.74)	2.89
TMS (0 – 4)	2.55 (0.67)	2.30 (0.60)	2.43
Curiosity	2.49 (0.87)	2.47 (0.78)	0.10
Decentering	2.60 (0.70)	2.15 (0.56)	7.88**
Testing Phase			
Low-cued ratings (0 – 100)			
Anticipatory Anxiety	15.47 (16.16)	20.11 (18.82)	1.09
Pain Intensity	32.97 (20.70)	28.97 (21.36)	0.56
Pain Unpleasantness	25.96 (19.66)	25.59 (20.97)	0.01
Novel-cued ratings (0 – 100)			
Anticipatory Anxiety	20.75 (18.15)	29.11 (20.52)	2.89
Pain Intensity	36.74 (21.18)	39.78 (19.61)	0.34
Pain Unpleasantness	29.80 (20.35)	36.92 (21.14)	1.83
High-cued ratings (0 – 100)			
Anticipatory Anxiety	20.87 (18.92)	30.99 (21.89)	3.79
Pain Intensity	44.23 (20.58)	44.65 (20.62)	0.01
Pain Unpleasantness	36.37 (22.10)	41.76 (21.82)	0.93
Manipulation Checks			
Confidence (1 - 5)	4.39 (1.02)	3.81 (1.01)	5.04*
Clarity (1 - 7)	5.77 (1.09)	6.23 (0.99)	2.93
Followed (1 - 7)	5.55 (0.99)	5.71 (1.07)	0.38
Ease (1 - 7)	5.16 (1.34)	5.00 (1.48)	0.20
Success (1 - 7)	5.10 (1.01)	5.39 (0.99)	1.31

SCS (Situational Catastrophizing Scale), TMS (Toronto Mindfulness Scale), Confidence (confidence in cue-stimulus contingency report), Clarity (clarity of instructions), Followed (extent to which instructions were followed), Ease (perceived ease in following instructions), Success (perceived successfulness in applying instructions); scale ranges are provided alongside each measure
Note: *** = p < .001, ** = p < .01, * = p < .05

2.4.3 Cue-induced anxiety and pain modulation: Mindfulness vs Suppression

Anticipatory Anxiety

The two-factor ANOVA conducted on the anticipatory anxiety ratings showed a significant main effect for Cue Type ($F(2,120) = 26.16$, $p < .001$, $\eta_p^2 = .30$) but not for Group ($F(1,60) = 2.74$, $p > .10$, $\eta_p^2 = .04$). Bonferroni-adjusted follow-up pairwise comparisons revealed lower anticipatory anxiety levels on the low-cued trials ($t(61)$ =

-5.36, $p < .001$) relative to the novel-cued trials, but no differences between high-cued and novel-cued trials ($t(61) = 0.83$, $p > .10$). There was also a marginal, but non-significant, Cue*Group interaction, $F(2,120) = 2.60$, $p = .08$, $\eta_p^2 = .04$. This marginal interaction was driven by marginally higher anticipatory anxiety ratings in the suppression group for novel-cued ($t(60) = 1.70$, $p = .09$) and high-cued trials ($t(60) = 1.95$, $p = .06$) relative to the mindfulness group, with no group differences observed for low-cued trials ($t(60) = 1.04$, $p = .30$).

Analyses of the computed difference scores for the anticipatory anxiety ratings revealed that the suppression group reported larger overall cued changes in anticipatory anxiety ratings than the mindfulness group, $F(1,60) = 5.84$, $p = .02$, $\eta_p^2 = .09$. We observed no significant Direction of modulation*Group interaction, $F(1,60) = 0.19$, $p > .10$, $\eta_p^2 = .003$.

Pain Intensity

Analyses of the pain intensity ratings again revealed a significant effect for Cue Type ($F(1.57,94.18) = 67.74$, $p < .001$, $\eta_p^2 = .53$) but no effect for Group ($F(1,60) = 0.001$, $p > .10$, $\eta_p^2 = .00$). The Bonferroni-corrected follow-up comparisons (($p = .05/2$) suggested that the paradigm was successful in inducing conditioned hypoalgesia and hyperalgesia, with low-cued trials resulting in lower pain intensity ratings ($t(61) = -6.30$, $p < .001$) and high-cued trials resulting in higher pain intensity ratings ($t(61) = 7.19$, $p < .001$), compared to novel-cued trials.

In addition, we also observed a significant Cue*Group interaction effect, $F(1.57,94.18) = 4.71$, $p = .02$, $\eta_p^2 = .07$. Bonferroni-corrected follow-up pairwise comparisons ($p = .05/4$) showed that low-cued trials resulted in significantly lower pain intensity ratings compared to novel-cued trials in the suppression group ($t(30) = -6.61$, $p < .001$), but failed to do so in the mindfulness group ($t(30) = -2.31$, $p = .07$). High-cued trials resulted in higher pain intensity ratings than the novel-cued trials in both the mindfulness ($t(30) = 6.17$, $p < .001$) and suppression group ($t(30) = 4.01$, $p < .001$).

Analyses of the computed difference scores for the pain intensity ratings revealed a significant Direction of modulation*Group interaction ($F(1,60) = 10.62$, $p < .01$, $\eta_p^2 = .15$), but no main effect for Direction of Modulation ($F(1,60) = 0.57$, $p > .10$, η_p^2

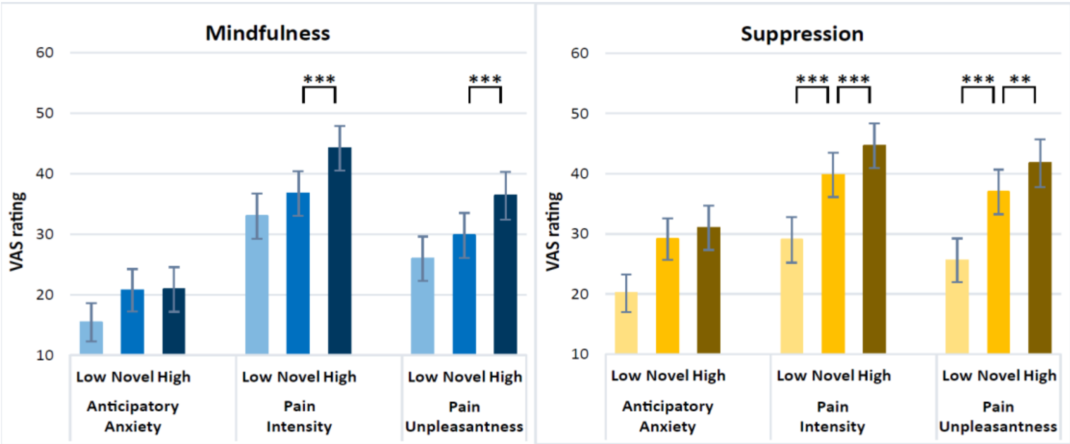
= .009) or Group (F(1,60) = 2.49, p > .10, η_p^2 = .04). Bonferroni-corrected follow-up pairwise comparisons (p = .05/2) showed reduced conditioned hypoalgesia magnitudes in the mindfulness compared to the suppression group, t(43.65) = -3.04, p < .01. There were no group differences in conditioned hyperalgesia magnitudes, t(60) = 1.53, p > .10.

Pain Unpleasantness

Analyses of the pain unpleasantness ratings revealed a significant effect for Cue Type (F(1.64,98.53) = 61.32, p < .001, η_p^2 = .51) but not for Group (F(1,60) = 0.62, p > .10, η_p^2 = .01). The main effect for Cue Type was again driven by lower pain unpleasantness ratings for low-cued trials (t(61) = -6.41, p < .001) and higher pain unpleasantness ratings for high-cued trials (t(61) = 6.05, p < .001), relative to novel-cued trials. There was a significant Cue*Group interaction, F(1.64,98.53) = 5.31, p = .01, η_p^2 = .08. Bonferroni-corrected (p = .05/4) follow-up comparisons revealed that the low-cued trials resulted in significantly lower pain unpleasantness ratings compared to novel-cued trials in the suppression group (t(30) = -6.77, p < .001), but not in the mindfulness group (t(30) = -2.29, p = .08). Both the mindfulness (t(30) = 4.93, p < .001) and suppression (t(30) = 3.62, p < .01) groups reported higher pain unpleasantness for high-cued trials, relative to the novel-cued trials.

Analyses of the computed difference scores for the pain unpleasantness ratings revealed a main effect for Group, with the suppression group reporting larger overall cue-induced changes in pain modulation than the mindfulness group (F(1,60) = 4.03, p = .049, η_p^2 = .06), but no main effect for Direction of Modulation (F(1,60) = 1.41, p > .10, η_p^2 = .02). More importantly, we observed a significant Direction of modulation*Group interaction effect, F(1,60) = 8.45, p < .01, η_p^2 = .12. Bonferroni-corrected follow-up pairwise comparisons (.05/2) showed smaller conditioned hypoalgesia magnitudes in the mindfulness compared to the suppression group, t(41.71) = -3.17, p < .01. There were no group differences in conditioned hyperalgesia magnitudes, t(60) = 0.92, p > .10.

Overall, while we observed cue-induced hyperalgesia in both groups, we found evidence for cue-induced hypoalgesia only in the suppression group. Importantly, there were no group differences on novel-cued trials, suggesting that the different patterns of results observed across the two groups were unlikely to be driven by differences in unconditioned pain ratings. Cue-induced anxiety, intensity and unpleasantness modulation across both groups are illustrated in Figure 2. Computed



hypoalgesia and hyperalgesia difference scores across both groups are illustrated in Figure 3.

Figure 2. Mean anticipatory anxiety, pain intensity and pain unpleasantness ratings on low, novel and high-cued trials across both groups. Error bars indicate standard errors. Note: *** = p < .001, ** = p < .01, * = p < .05

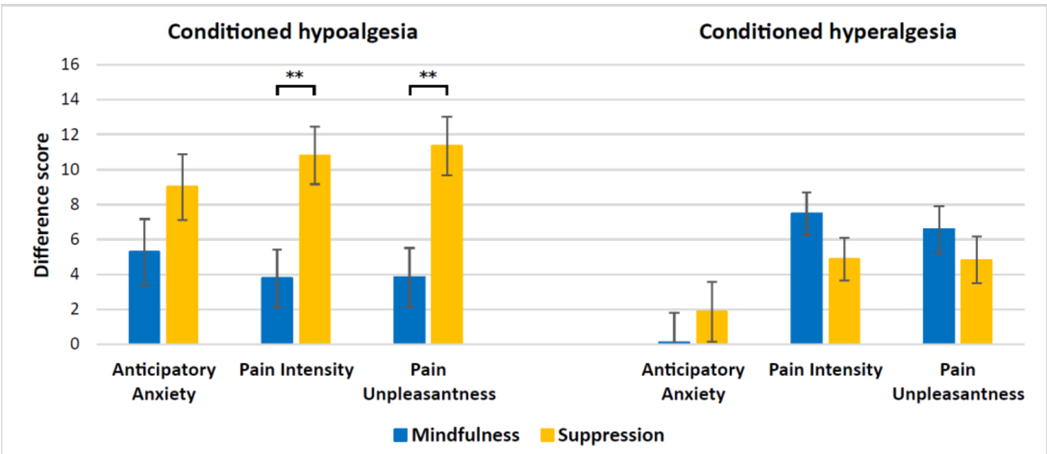


Figure 3. Computed conditioned hypoalgesia and hyperalgesia magnitudes (using a difference score approach) across both groups. Error bars indicate standard errors. Note: *** = p < .001, ** = p < .01, * = p < .05

2.4.4 Cue-induced anxiety and pain modulation: Associations with trait and state mindfulness and pain catastrophizing measures

We first ran preliminary two-tailed Pearson correlations to test for any significant association between the self-report mindfulness and pain catastrophizing questionnaires and the VAS ratings on the (unconditioned) novel-cued trials. The analyses revealed a significant negative correlation between state mindfulness scores and state pain catastrophizing scores ($r = -.41$, $p = .001$). Importantly, higher levels of state mindfulness were associated with lower anticipatory anxiety ($r = -.44$, $p < .001$), pain intensity ($r = -.29$, $p = .02$) and pain unpleasantness ($r = -.31$, $p = .01$) ratings. In contrast, higher state pain catastrophizing levels were associated with increased anticipatory anxiety ($r = .37$, $p < .01$), pain intensity ($r = .35$, $p < .01$) and pain unpleasantness ($r = .43$, $p < .001$) ratings. We also observed a significant negative correlation between trait mindfulness and trait pain catastrophizing ($r = -.26$, $p = .04$). However, neither measure correlated significantly with the outcome or state self-report measures (p's all > .10). Subsequent partial correlational analyses (controlling respectively for anxiety, intensity and unpleasantness ratings on novel-cued trials) revealed that higher state mindfulness scores were linked to higher pain intensity ratings on the low-cued trials (i.e., reduced cue-induced hypoalgesia) but lower anticipatory anxiety levels on the high-cued trials (see Table 3). Conversely, state catastrophizing was associated with increased anticipatory anxiety and pain intensity ratings for the high-cued trials (i.e., increased cue-induced hyperalgesia).

Finally, correlational analyses conducted on the computed difference scores revealed a similar pattern of results (see Table 4). Higher state mindfulness scores were associated with smaller conditioned hypoalgesia magnitudes for pain intensity ratings and marginally smaller hypoalgesia magnitudes for the pain unpleasantness ratings ($p = .08$). Higher levels of state pain catastrophizing were associated with larger conditioned hyperalgesia magnitudes for the anticipatory anxiety ratings.

Table 3. Partial correlations (controlling for novel-cued trials) between the self-report questionnaires and VAS ratings on low and high-cued trials.

	Low pain cue			High pain cue		
	Anxiety	Intensity	Unpleasantness	Anxiety	Intensity	Unpleasantness
TMS	-.12	.28*	.14	-.29*	-.06	-.13
Curiosity	-.11	.17	.05	-.24	-.09	-.17
Decentering	-.10	.32*	.19	-.25	-.01	-.06
State Pain	.26*	-.10	-.11	.33**	.27*	.22
Catastrophizing	-.07	-.04	-.12	.02	.12	.03
FFMQ	.03	-.10	-.11	-.08	.13	.07
PCS						

TMS = Toronto Mindfulness Scale (state mindfulness). Note: *** = p < .001, ** = p < .01, * = p < .05

Table 4. Correlations between the self-report questionnaires and the computed difference scores.

	Conditioned hypoalgesia			Conditioned hyperalgesia		
	Anxiety	Intensity	Unpleasantness	Anxiety	Intensity	Unpleasantness
TMT	-.10	-.31*	-.22	-.21	-.01	-.12
Curiosity	-.06	-.20	-.13	-.19	-.05	-.15
Decentering	-.13	-.35**	-.26*	-.17	.04	-.05

State Pain	-.05	.15	.23	.27*	.20	.19
Catastrophizing	.00	.06	.14	.03	.09	.02
FFMQ	.05	.08	.09	-.10	.15	.07
PCS						

TMT = Toronto Mindfulness Scale (state mindfulness). Note: *** = $p < .001$, ** = $p < .01$, * = $p < .05$.

2.5 Discussion

The current study aimed to investigate how instructed use of a mindfulness or a suppression strategy modulates pain perception during a classical pain conditioning task. The findings partially support the hypothesis that a brief mindfulness induction reduces sensitivity to pain-cueing procedures. While we found evidence for conditioned hyperalgesia in both the mindfulness and suppression groups, only the latter reported lower pain intensity and pain unpleasantness ratings on the low-cued trials (i.e., conditioned hypoalgesia).

The absence of conditioned hypoalgesia in the mindfulness condition could be construed as indicative of reduced effectiveness in pain attenuation, relative to the suppression condition. This interpretation, however, is inconsistent with the lower, albeit non-significant, pain ratings reported by the mindfulness group on the unconditioned (novel-cued) trials. Previous studies comparing mindfulness and suppression strategies have likewise either reported no group differences in unconditioned pain ratings or reduced pain ratings in their mindfulness condition (Kohl et al., 2012). We would argue, therefore, that the lack of conditioned hypoalgesia in the mindfulness condition is instead a by-product of contrasting mechanisms underlying mindfulness-driven vs. conditioning/expectancy-driven pain modulation. This argument is supported by neuroimaging evidence showing that pain alleviation during mindfulness is associated with a pattern of neural activity opposite to that observed in placebo hypoalgesia (Zeidan et al., 2015). Furthermore, recent studies have shown that while administration of an opioid antagonist (naloxone) was successful in nullifying hypoalgesic effects induced by a placebo saline infusion, the antagonist failed to reverse mindfulness-induced hypoalgesia (Wells et al., 2020; Zeidan et al., 2016). These findings suggest that mindfulness may alleviate pain via unique neuropsychological mechanisms which bypass opioidergically mediated descending pathways typically involved in the cognitive modulation of pain (King et al., 2013; Sprenger et al., 2012).

Nevertheless, while the results supported our prediction of reduced conditioned hypoalgesic effects following mindfulness training, we failed to observe the hypothesised mindfulness-induced reductions in conditioned hyperalgesia. These asymmetrical findings may have resulted from the disparate neuropsychological mechanisms underlying conditioned hypoalgesia vs. conditioned hyperalgesia. Freeman et al. (2015) previously demonstrated that, while behavioural responses evoked by placebo and nocebo procedures are significantly correlated, placebo conditioning elicited changes in the insula, orbitofrontal cortex, and periaqueductal gray while nocebo conditioning was linked to altered striatal activity, with no overlapping activation across the two conditions. Alternatively, the preserved conditioned hyperalgesia may also be explained by an increased difficulty in modulating nocebo-like effects. Previous studies have shown conditioned nocebo effects to be significantly more resistant to extinction than conditioned placebo effects (Colagiuri et al., 2015; Colloca et al., 2008), presumably due to the higher adaptive cost associated with information about impending threat (i.e., high pain cue). It is, however, important to highlight the limited generalizability of the current mindfulness manipulation to the practice and construct of mindfulness as a whole. Our brief mindfulness induction is unlikely to capture the full phenomenological complexity of mindfulness as experienced by expert practitioners or even novice practitioners who have completed introductory mindfulness-based courses. Accordingly, it must be noted that the mindfulness group scored higher than the suppression group on the decentering subscale, but not on the overall state mindfulness measure. This may potentially be explained by the fact that the TMS was administered as a retrospective measure after the testing phase of the study, rather than immediately after the mindfulness induction, as is common practice. Furthermore, Ireland et al. (2019) recently raised some doubts as to the sensitivity of the curiosity subscale of the TMS in assessing potential group differences, which may explain why we only observed group differences on the decentering subscale. Nevertheless, concerns may be raised as to the extent to which mindfulness was successfully induced, and if so, whether the observed results may have been driven by some extraneous variables. However, we think this is unlikely given that the correlational analyses conducted between the state mindfulness scores and conditioned hypoalgesia and hyperalgesia revealed a similar pattern of results, irrespective of group membership. Higher state mindfulness levels were associated with reduced conditioned hypoalgesia for pain intensity ratings (and marginally reduced conditioned hypoalgesia for unpleasantness ratings), but not with conditioned hyperalgesia. Nevertheless, we cannot rule out the possibility that a sample of experienced mindfulness practitioners may show improved resistance to conditioned hyperalgesia. Recent evidence from Taylor et al. (2018) showing that experienced meditators (>1000 hours of practice) exhibit reduced conditioned hyperalgesic effects compared to meditation-naïve controls during a classical fear-conditioning paradigm suggests that this may indeed be the case. Importantly, meditators did not differ from controls in nocifensive reflexes elicited by the conditioned cues, suggesting that meditation experience does not weaken the critical ability to learn from associative cues. The authors argued that meditation may instead reduce cue-induced pain modulation by limiting the influence of such associative learning and anticipation on pain perception.

Some further limitations of the current study also need to be acknowledged. Firstly, we did not include a (no-instructions) control group. We opted to use a suppression condition as our comparison group to minimise the potential heterogeneity in coping strategies that is likely to arise from a no-instructions group condition (Van Ryckeghem et al., 2018). The downside to this approach, however, is that it does not allow for any definitive conclusions to be drawn regarding the directional influence of the two conditions. In other words, inclusion of a no-instructions group would be necessary to determine whether the group differences in conditioned hypoalgesia were driven by reduced sensitivity to conditioning procedures during mindfulness, increased sensitivity during suppression or a combination of both. Likewise, it would be important to extend the paradigm to other forms of cognitive strategies (e.g., reappraisal, distraction, hypnosis) to determine whether the observed modulatory effects are unique to mindfulness. Secondly, unconditioned pain ratings were assessed on the premise that responses on novel-cued trials should be free from any influence of the conditioning procedure. Although the introduction of novel cues is common practice in classical conditioning paradigms, it cannot be fully ruled out that participants may have assumed the novel cue to be predictive of an intermediate temperature level.

Notwithstanding the aforementioned caveats, our findings, together with those of Taylor et al. (2018), provide initial support for the notion that mindfulness may minimize the biasing influence of expectations on pain perception. Recently formulated predictive coding models provide a promising unifying framework within which to explore the interplay between prior expectations (i.e., predictive value of the conditioned cues), sensory information (i.e., heat stimulation) and (mindful) attention modulation (Farb et al., 2015; Lutz et al., 2019; Pagnoni, 2019). According to these models, the key prescriptions of heightened sustained attention towards current sensory experience during mindfulness practice, coupled with increased stability in interoceptive and proprioceptive anchoring (via immobility of posture and gaze), may result in an increase in the precision of ascending sensory information. Conversely, the reallocation of attention from habitually activated mental content (e.g., during mind-wandering) to the non-elaborative monitoring of arising sensations and thoughts should lead to a curtailing of top-down mental processes fuelled by expectations, desires and schemas. Together, these effects may combine so that perceptual experience in mindfulness is less likely to be shaped by prior expectations and beliefs (i.e., descending predictions from higher cortical areas (Atlas & Wager, 2012)). This interpretation is also consistent with the unique neural pattern of reduced prefrontal activity and increased sensory processing-related activity observed in neuroimaging studies of mindfulness-induced hypoalgesia (Gard et al., 2011). Nevertheless, further research is required to substantiate this purported link between these neural mechanisms to the pain conditioning effects observed here. In line with previous reports that reduced functional connectivity between executive and sensory-related brain areas are associated with increased pain tolerance in mindfulness practitioners (Grant et al., 2011), we would expect similar functional decoupling to also predict the reduced cue-induced pain modulation observed here. Nonetheless, it is important to note that while the current evidence is consistent with the predictive processing view of mindfulness, the study did not aim to provide a direct test of the mechanistic postulates derived from these models. For instance, reduced cue-induced hypoalgesia, as per this framework, could be explained by either higher weighting of afferent sensory information, lower weighting of prior information or an integration of both mechanisms. Our paradigm, however, does not allow us to tease apart the relative contributing influence of these different processes. Computational modelling of trial-by-trial changes in conditioned pain ratings based on the tenets of predictive coding (e.g., Hoskin et al., 2019) and effective connectivity studies of related neural activity (e.g., Sevel et al., 2015) provide promising pathways towards addressing these research questions.

While the hypoalgesic effects of mindfulness practice have been the subject of increasing empirical interest, the current study offers a first glimpse into how pain modulation may in itself deepen our understanding of the underlying mechanisms of mindfulness. Importantly, our findings provide novel evidence suggesting that mindfulness and expectancy-driven hypoalgesia may not only involve contrasting, but also counteracting, mechanisms. Nevertheless, the merging of pain cueing paradigms with neuroimaging and computational modelling techniques in samples of experienced practitioners represent important steps in advancing this line of investigation.

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3 STUDY II: Categorization Alters Perception: The Pervasive Biasing Influence of Category Labels on Pain Perception and Decision-Making

3.1 Abstract

Evidence from a recently developed pain categorization paradigm suggests that providing implicit categorical information about painful stimuli can significantly influence pain reports. Given the clinical relevance of these findings for medical diagnostics, it is important to identify potential predictors or moderators of categorization-induced biases. Across two separate studies, we first aimed to provide a proof-of-concept replication of the paradigm and then tested whether categorization effects could be modulated by trait mindfulness level. In the first study, participants were assigned to either a categorization condition (with stimuli labels suggestive of a categorical distinction between higher and lower pain stimuli) or a control condition (with stimuli labels suggestive of a continuum of pain stimuli). The categorization group reported lower within-category variability and higher between-category variability for the pain unpleasantness ratings. The categorization group was also more likely to confuse within-category stimuli than between-category stimuli, relative to the control group. In the second study, we compared high and low trait mindfulness scorers who were both assigned to the categorization condition from the first study. Magnitudes of categorization-induced effects did not differ across the two groups. The findings replicated previous evidence that categorization can lead to increased perceived similarity for stimuli within-category, and reduced similarity for stimuli between categories. We explore potential reasons for the lack of modulatory influence of trait mindfulness level and discuss clinical implications of the pervasiveness of categorization biases.

3.2 Introduction

Categorization is a fundamental cognitive ability that helps in optimizing perceptual efficiency in a world laden with sensory information. Grouping stimuli into categories not only facilitates the structuring of sensory input with minimal cognitive effort, but also allows both inferences about unobserved features of a stimulus based on its category membership and the rapid integration of novel stimuli based on their characteristics. However, despite its adaptive properties, the simplification that underlies categorization processes can also lead to poorer differentiation of stimuli falling within the same category (i.e., assimilation effect) and exaggerated discrimination of stimuli attributed to separate categories (i.e., accentuation effect). Such perceptual categorization effects have previously been observed for visual (Corneille et al., 2002; Goldstone, 1995; Tajfel & Wilkes, 1963), auditory (Campbell et al., 1956), haptic (Gaißert et al., 2011), social (Etcoff and Magee, 1992; Rubin and Badea, 2012), and more recently interoceptive (Petersen et al., 2014, 2015) stimuli.

However, the influence of categorization processes in the nociceptive realm has received little attention so far in the empirical literature. To date, a single published study has investigated potential categorization-induced biases in pain perception. Van der Meulen et al. (2017) introduced a novel pain categorization paradigm during which they administered a series of heat stimuli which were equidistant in temperature. The heat stimuli were either artificially grouped into two categories (i.e., categorization condition) or presented along a continuum (i.e., control condition). This manipulation resulted in increased similarity in pain unpleasantness ratings for stimuli within similar categories (i.e., assimilation) and reduced similarity for stimuli assigned to separate categories (i.e., accentuation). Furthermore, participants in the categorization condition were more likely to confuse stimuli within categories than between categories. These findings hold important clinical implications given the common use of categorical pain labels (e.g., mild vs. severe, dull vs. sharp) in medical diagnostics. Poorer perceptual differentiation between painful sensations can, for instance, result in the overlooking of potentially serious symptoms, over-generalization of pain-related fear and maladaptive coping behaviours (Cronje and Williamson, 2006; Zaman et al., 2015; Bennett et al., 2015). These findings are also in line with the well-documented biasing influence of prior expectations or information (i.e., the category labels in the current instance) on pain perception (Villemure and Bushnell, 2002; Tracey, 2010; Wiech, 2016). Given the potentially detrimental consequences associated with misperception and misattribution of bodily sensations (De Peuter et al., 2011; Di Lernia et al., 2016), it is essential to determine the extent to which these categorization-induced biases can be modulated and identify potential factors and strategies that can help in minimizing or countering these effects.

Mindfulness-based interventions may provide a potentially promising avenue in that regard. Recent neuroimaging-informed theoretical accounts of mindfulness suggest that the non-judgmental and non-elaborative form of awareness towards ongoing sensory experience that mindfulness practice encourages may help preserve perceptual objectivity in the face of contradicting beliefs and expectations. Accordingly, we recently found supporting evidence that brief mindfulness practice may indeed reduce sensitivity to pain conditioning procedures during a classical pain cueing study (Vencatachellum et al., 2021). Similar findings have also been reported in samples of experienced meditators (Taylor et al., 2018). Therefore, it seems plausible to expect a similar protective effect of mindfulness against the biasing influence of category labels on pain perception.

We investigated this possibility across two separate studies. Study 2(a) aimed to replicate the assimilation and accentuation effects observed by van der Meulen et al. (2017), using a slightly modified version of the pain categorization paradigm. In Study 2(b), we aimed to test whether the magnitude of these effects could be modulated by trait mindfulness levels.

3.3 Methods (STUDY A)

3.3.1 Participants

Participants were recruited via an online University platform dedicated to participant recruitment. All study volunteers completed a screening procedure assessing eligibility for participation prior to the study. Exclusion criteria included: presence of acute pain, joint or muscle problems, current or past history of chronic pain, skin or neurological conditions, and current intake of pain or related medication. Fifty participants met the eligibility criteria for the study. Two of these participants however failed to complete the laboratory session and were excluded from the data analyses, leaving a sample of 48 participants (65% female) aged from 19 to 32 years old (M = 23.04, SD = 2.91). They were randomly assigned to either a categorization group (N = 26) or a control group (N = 22), using a permuted block randomization (ABBA) approach. All participants provided written informed consent prior to the study and were remunerated either via course credit or 15€ worth of gift vouchers. The experimental protocol was approved by the ethics committee of the University of Luxembourg (ref: ERP 20-007).

3.3.2 Pain categorization paradigm

The pain categorization paradigm consisted of a learning phase and a recall phase. In the learning phase, participants received a series of six heat stimuli, spanning a temperature range of 2.5°C in increments of 0.5°C (e.g., 45°C, 45.5°C, 46°C, 46.5°C, 47°C and 47.5°C). The temperatures administered were derived individually for each participant based on their pain tolerance level (see pain stimulation section). Each of the stimuli was presented alongside its own unique label. In the categorization condition, the six stimuli were labelled A1, A2, A3, B1, B2 and B3 (in linear ascending order from lowest to highest temperature). This procedure helps create an implicit category border between the lower temperature range (i.e., A1, A2, A3) and the higher temperature range (i.e., B1, B2, B3). To further enhance the categorical distinction, stimuli A1, A2 and A3 were presented in blue font while stimuli B1, B2 and B3 were presented in red font. In the control condition, the six stimuli were instead labelled S1, S2, S3, S4, S5 and S6 (again in linear ascending order from lowest to highest temperature), thereby implying a continuum of stimulus intensity. All stimuli in the control group were presented in purple font. Overall, the learning phase comprised 24 trials (four of each stimulus type) presented in a pseudo-random order. Participants were required to rate the level of pain intensity and pain unpleasantness that they experienced during each trial, using two 100-point VAS scales (0 = 'not intense/unpleasant at all' to 100 = 'extremely intense/unpleasant').

In the recall phase, the same six stimuli were presented without their labels and participants were required to identify the corresponding label for the presented stimulus. In addition, participants were asked to rate their confidence level in their response on a 100-point VAS scale (0 = 'not confident at all' to 100 = 'extremely confident') after each trial. The recall phase comprised 36 trials (six of each stimulus type) presented in a pseudo-random order. Figure 1 provides a schematic representation of stimuli examples and trial timeline across the learning and recall phases.

(a)

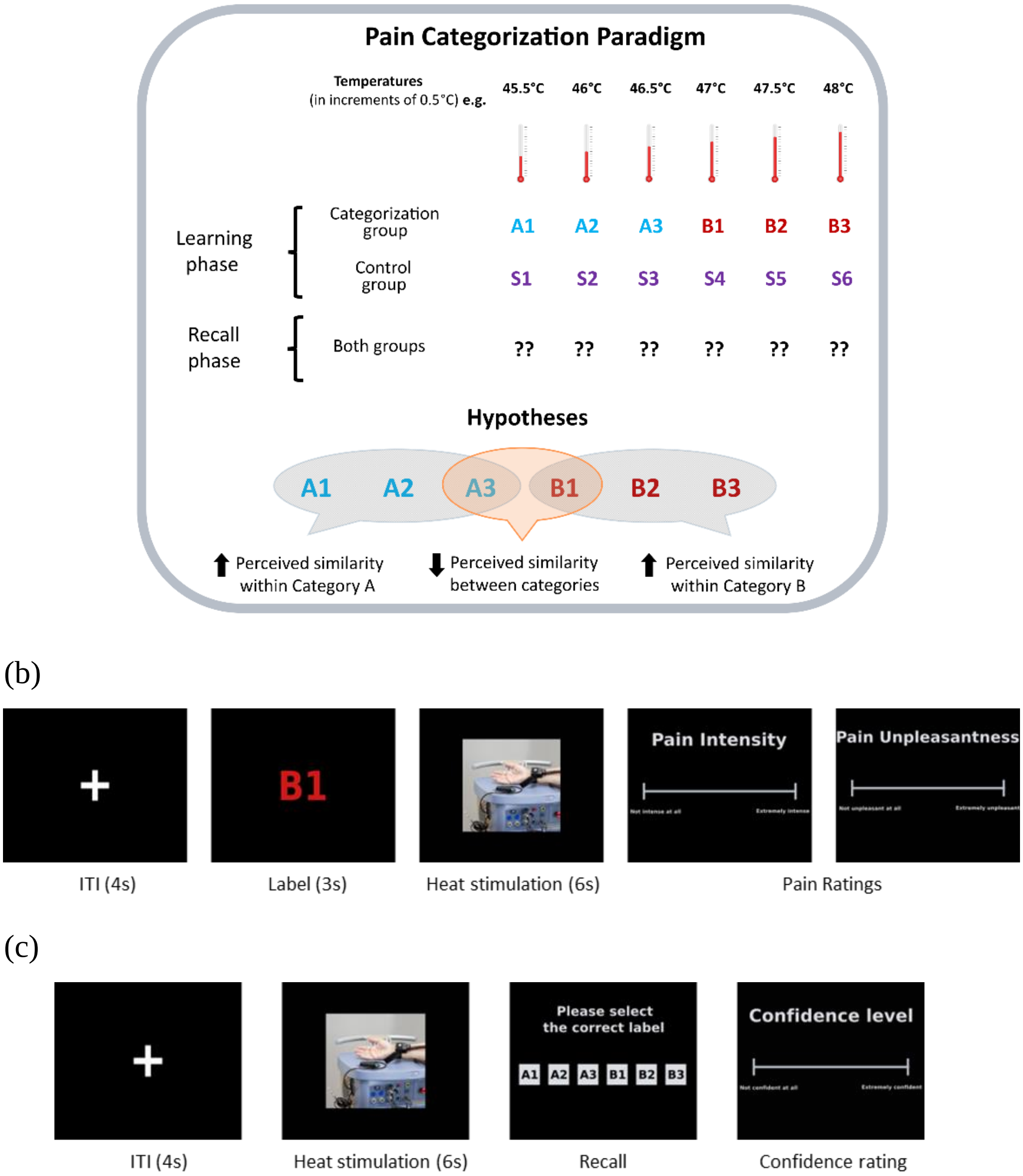

Figure 1. (a) Schematic representation of stimuli examples across the learning and recall phases and derived hypotheses; (b) Time-course for a typical trial within the learning phase; (c) Time-course for a typical trial within the recall phase.

3.3.3 Pain stimulation

Pain stimuli were administered via a contact thermal heat stimulator (Somedic AB, Sweden). The 25 x 50 mm thermode was positioned on the volar surface of the participant's left forearm. We conducted a pain calibration procedure at the beginning of the session to derive a range of temperatures in line with each participant's pain sensitivity. During the calibration, participants were presented with three practice trials followed by a pseudo-random series of 18 heat stimuli, ranging from 44°C to 49°C. Participants were asked to rate the level of pain they experienced for each stimulus on a VAS scale (0 = 'No pain' to 100 = 'Unbearable pain'). We fitted a sigmoid (Weibull) stimulus-response curve (Yoshida et al., 2013) to the participant's ratings, from which we derived the temperature level that was predictive of a pain rating of 60 on the VAS scale. This temperature level was used for the B1/S4 stimulus during the pain categorization paradigm. We then added and subtracted increments of 0.5°C to and from the derived B1/S4 stimulus intensity to obtain the temperature levels for the five other stimuli (see an example of derived temperatures in Figure 1(a), with 47°C as temperature for the B1/A4 stimulus). As such, the temperature range always spanned 2.5°C for all participants. The pain stimulation lasted 6 s (ramp up:1.5 s, plateau:3 s, ramp down:1.5 s), with a baseline temperature of 35°C.

3.3.4 Session procedure

Participants provided written informed consent at the beginning of the study. The experimental session was conducted in a laboratory room specifically dedicated to experimentally-induced pain research. Participants were seated in a reclining chair around 100cm away from a 24-inch screen monitor and used a mouse to respond to all study items. We first conducted the pain calibration procedure to derive individual temperatures for the six heat stimuli. Participants then completed the learning phase of the pain categorization task. They were explicitly informed that the same heat stimuli would be presented without their respective labels later during the recall phase, and that they would be required to identify the corresponding label for each stimulus. The learning phase was followed by a short self-timed break, after which participants completed the recall phase of the paradigm. They were fully debriefed as to the purpose of the study at the end of the session.

3.3.5 Data analysis

For data analytic purposes, stimuli labels used in the categorization and control groups were treated identically, i.e., stimuli A1-A3 and S1-S3 were construed as belonging to the same Category A and stimuli B1-B3 and S4-S6 were construed as belonging to the same Category B.

For the learning phase, we were specifically interested in the extent to which stimuli within a specific category were perceived as similar to each other, relative to stimuli belonging to separate categories. To do so, we computed intra-individual variability in pain ratings for stimuli within and between categories, using a similar approach to that employed by van der Meulen et al. (2017). We first calculated for each participant the average pain intensity and pain unpleasantness ratings for each of the six stimuli. As a second step, we computed the standard deviations in ratings for stimuli within categories A (SD_A) and B (SD_A), and in ratings for stimuli at the category border (i.e., A3-B1 or S3-S4; SD_{AB}) individually for each participant. For easier interpretability, we normalized the intra-individual variability scores by dividing the computed standard deviations by the number of measurements they were based on (i.e., three for SD_A and SD_B, and two for SD_{AB}). Lower intra-individual variability scores are indicative of increased perceived similarity. We performed a two-way ANOVA on the intra-individual variability scores, with Group (categorization vs. control) as the between-subjects factor and Category (SD_A vs. SD_{AB} vs. SD_B) as the within-subject factor. As we hypothesized that the category labels (in the categorization group) should lead to increased perceived similarity for stimuli within categories and reduced perceived similarity for stimuli between categories, we expected to observe a quadratic Group x Category interaction effect.

For the recall phase, we computed confusion frequencies for stimuli within and between categories using a generalization index 'g' (Shepard, 1987). More specifically, the index was computed by dividing the proportion of trials in which adjacent stimuli were confused with each other by the proportion of correct responses, e.g., for the adjacent pair A1-A2, we calculated the proportion of trials whereby A1 was confused with A2 and A2 was confused with A1 and divided it by the proportion of aggregated correct identifications for A1 and A2. We then computed the within-category confusion indices for category A (i.e., g_A) and B (i.e., g_B) by averaging the g indices for the corresponding adjacent pairs (i.e, A1-A2 and A2-A3 for $g_{A,}$ and B1-B2 and B2-B3 for $g_{B,}$ within the categorization condition). Between-category confusion (g_{AB}) was calculated from the relative confusion and correct identification frequencies for the adjacent stimuli pair A3-B1 (or S3-S4 for the control group). The 'g' index hence also acts as a proxy for perceived similarity; stimuli that are perceived as more similar to each other are more likely to evoke equivalent responses (i.e., be confused with each other). Higher 'g' values reflect higher confusion frequencies relative to correct identifications (i.e., increased perceived similarity). We performed a two-way ANOVA on the confusion frequencies, with Group (categorization vs. control) as the between-subjects factor and Category (g_A vs. g_{AB} vs. g_B) as the within-subject factor. We again expected to observe a quadratic Group x Category interaction effect, with higher within-category confusion frequency and lower between-category confusion frequency levels in the categorization group.

Finally, we performed two separate two-way ANOVAs on the confidence ratings for stimuli from Category A and stimuli from Category B respectively. Group (categorization vs. control) was the between-subjects factor and Stimulus (A1/S1 vs. A2/S2 vs. A3/S3 or B1/S4 vs. B2/S5 vs. B3/S6) was the within-subject factor. We expected to observe a trend toward higher confidence ratings for stimuli at the category border (i.e., A3/S3 and B1/S4) and lower confidence ratings for the other four stimuli in the categorization group, relative to the control group.

We also conducted follow-up pairwise comparisons for the aforementioned analyses to probe potential interaction effects. Greenhouse-Geisser corrections were used wherever assumptions of sphericity was violated and Sidak corrections were applied to adjust for multiple comparisons.

3.4 Results (STUDY A)

3.4.1 Group characteristics

The categorization and control groups did not differ in terms of gender distribution ($\chi 2(1, N = 48) = .67$, p = .41) or age ($t(46) = 0.80$, $p = .43$). The two groups also did not differ with regards to the stimuli temperatures used during the pain categorization task, ($t(46) = 0.12$, $p > .05$).

3.4.2 Learning phase

Pain intensity and unpleasantness ratings

A two (Group) x six (Stimuli) mixed ANOVA conducted on the pain intensity ratings revealed a significant main effect of Stimuli ($F(2.62,120.68) = 174.07$, $p < .001$, $\eta_p^2 = .79$), but no significant Group effect ($F(1,46) = 1.55$, $p = .22$, $\eta_p^2 = .03$) or Group x Stimuli interaction effect ($F(2.62,120.68) = 2.05$, $p = .12$, $\eta_p^2 = .04$). Follow-up pairwise comparisons confirmed that there were significant differences in intensity ratings between each adjacent pair of stimuli (e.g., A1 vs. A2), $t(47)$'s ranging from 5.98 to 9.19, p's all < .001.

The analysis was repeated on pain unpleasantness ratings and again revealed a significant main effect of stimuli (*F*(2.46,113.14) = 167.40, $p < .001$, $\eta_p^2 = .78$), but no significant Group effect (*F*(1,46) = 0.67, $p = .42$, $\eta_p^2 = .01$) or Group x Stimuli interaction effect (*F*(2.46,113.14) = 1.49, $p = .23$, $\eta_p^2 = .03$). The follow-up pairwise comparisons again showed that each adjacent pair of stimuli differed significantly in pain unpleasantness ratings (*t*(47)'s ranging from 4.77 to 7.88, *p*'s all < .001). These results confirm that participants successfully detected the increase in temperatures across stimuli. Pain intensity and unpleasantness ratings across groups and stimuli are depicted in Tables 1 and 2.

Table 1. Mean (SD) and *t* values for pain intensity ratings.

	Pain Intensity (0 -100)					
	A1	A2	A3	B1	B2	B3
Control	13.19 (14.07)	27.11 (18.10)	39.97 (17.85)	51.11 (16.46)	63.35 (18.43)	76.24 (19.13)
Categorization	14.78 (13.52)	26.22 (15.19)	33.56 (17.43)	44.80 (18.00)	55.29 (18.88)	65.64 (20.15)
t(46)	-.40	0.19	1.26	1.26	1.49	1.86

Table 2. Mean (SD) and *t* values for pain unpleasantness ratings.

	Pain Unpleasantness (0 – 100)					
	A1	A2	A3	B1	B2	B3
Control	10.40 (12.37)	18.78 (13.59)	30.57 (16.23)	41.76 (18.69)	54.39 (21.36)	68.93 (23.38)
Categorization	10.52 (10.79)	20.01 (14.14)	26.01 (15.24)	39.22 (17.33)	49.96 (17.89)	59.47 (19.50)
t(46)	-0.04	-0.31	1.00	0.49	0.78	1.51

3.3.3 Intra-individual variability in pain ratings

The two-way ANOVA conducted on intra-individual variability in pain intensity ratings revealed no significant effects of Group (*F*(1,46) = 3.64, $p = .06$, $\eta_p^2 = .07$) or Category (*F*(1.60,73.49) = 1.25, $p = .29$, $\eta_p^2 = .03$). We also failed to observed any quadratic Group x Category interaction effect (*F*(1,46) = 0.93, $p = .34$, $\eta_p^2 = .02$).

The two-way ANOVA conducted on intra-individual variability in pain unpleasantness ratings revealed a significant main effect of Category (*F*(1.73,79.42) = 3.81, $p = .03$, $\eta_p^2 = .08$) but no significant effect of Group (*F*(1,46) = 0.52, $p = .47$, η_p^2

= .01). Follow-up pairwise comparisons showed that the Category effect was driven by marginally higher intra-individual variability scores for stimuli at the category border (SD_{AB}) relative to stimuli within Category A (SD_A), $t(47) = 2.42$, $p = .06$. More importantly, we also observed a significant quadratic Group x Category interaction effect, $F(1,46) = 7.67$, $p = < .01$, $\eta_p^2 = .14$. Follow-up pairwise comparisons further showed that the categorization group reported marginally higher SD_{AB} variability scores ($t(46) = 1.73$, $p = .09$), but marginally lower SD_A ($t(46) = 1.89$, $p = .07$) and significantly lower SD_B variability ($t(46) = 2.18$, $p = .03$), relative to the control group.

In line with our hypothesis, the category labels led to lower variation in pain unpleasantness ratings (i.e., increased perceived similarity) for stimuli within categories and higher variation in unpleasantness ratings (i.e., reduced perceived similarity) for stimuli between categories. We observed a similar trend for pain intensity ratings, but that pattern did not reach significance. Intra-individual variability for pain intensity and pain unpleasantness across groups and categories are depicted in Figure 2.

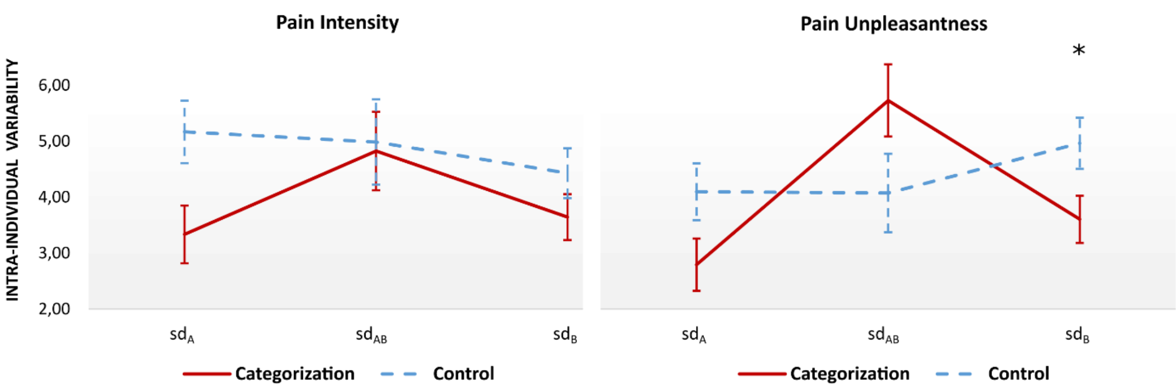

Figure 2. Intra-individual variability in pain intensity and unpleasantness ratings across groups and categories. Error bars are indicative of the standard errors.

3.3.4 Recall phase

Confusion frequencies

The two-way ANOVA conducted on the computed confusion frequencies revealed a significant Category effect ($F(2,92) = 3.38$, $p = .04$, $\eta_p^2 = .07$) but no group effect ($F(1,46) = 0.94$, $p = .76$, $\eta_p^2 = .002$). Follow-up pairwise comparisons showed lower confusion frequencies for stimuli within category B (g_B) relative to within category A (g_A), $t(47) = -2.60$, $p = .04$. Crucially, we also found a significant quadratic Group x Category interaction effect, $F(1,46) = 10.02$, $p < .01$, $\eta_p^2 = .18$, showing the hypothesized trend of higher confusion frequencies for stimuli within categories relative to between categories in the categorization group (and the opposite trend in the control group). Follow-up pairwise comparisons further revealed significantly higher confusion frequencies for stimuli between categories (g_{AB}) in the control group relative to the categorization group, $t(46) = 2.35$, $p = .02$, but no significant group differences in g_A or g_B (p's all > .10). Confusion frequencies across groups and categories are depicted in Figure 3.

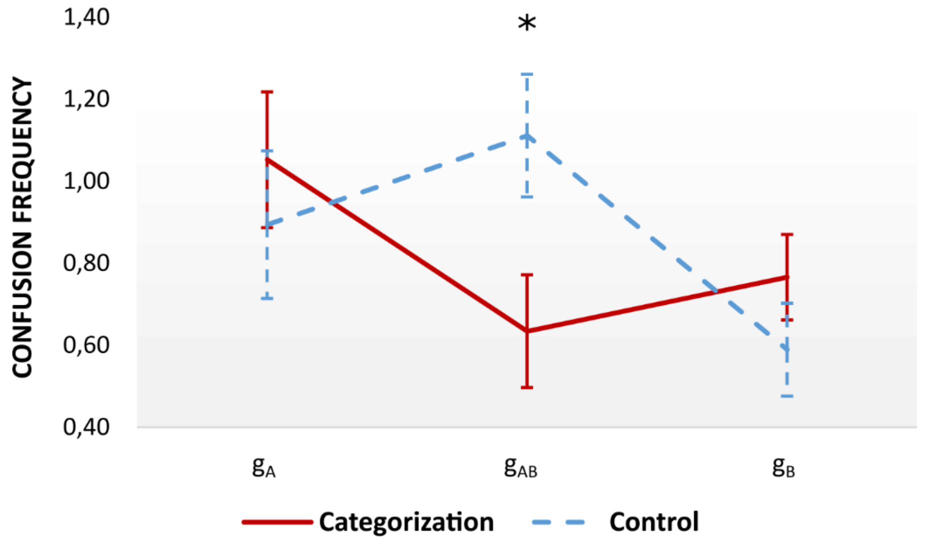

Figure 3. Confusion frequencies across groups and categories. Error bars are indicative of the standard errors.

Confidence ratings

The two-way ANOVA conducted on the confidence ratings for stimuli in Category A revealed a marginally significant effect of Stimulus ($F(2,92) = 2.97$, $p = .06$, $\eta_p^2 = .06$) but no Group effect ($F(1,46) = 0.16$, $p = .69$, $\eta_p^2 = .004$). Follow-up pairwise comparisons revealed that confidence ratings were marginally higher for A1 compared to A3, $t(47) = 2.34$, $p = .07$, with no differences for the other pairwise comparisons, p's all > .10. We found no Group x Stimulus interaction effect, $F(2,92) = 1.17$, $p = .32$, $\eta_p^2 = .03$.

The two-way ANOVA conducted on the confidence ratings for stimuli in Category B revealed a significant effect of Stimulus ($F(1.75,80.59) = 39.33$, $p < .001$, $\eta_p^2 = .46$) but no Group effect ($F(1,46) = 0.01$, $p = .92$, $\eta_p^2 = .00$). Follow-up pairwise comparisons revealed that confidence ratings for B2 were marginally higher than for B1 ($t(47) = 2.46$, $p = .05$) but significantly lower than for B3 ($t(47) = -7.30$, $p < .001$). We also found a marginally significant Group x Stimulus interaction effect, $F(1.75,80.59) = 3.09$, $p = .06$, $\eta_p^2 = .06$. The interaction was driven by significantly higher confidence ratings for B2/S5 relative to B1/S4 in the control group ($t(21) = 3.36$, $p < .001$), but not in the categorization group ($t(25) = -0.15$, $p = 0.99$). Confidence ratings across groups and stimuli can be found in Figure 4.

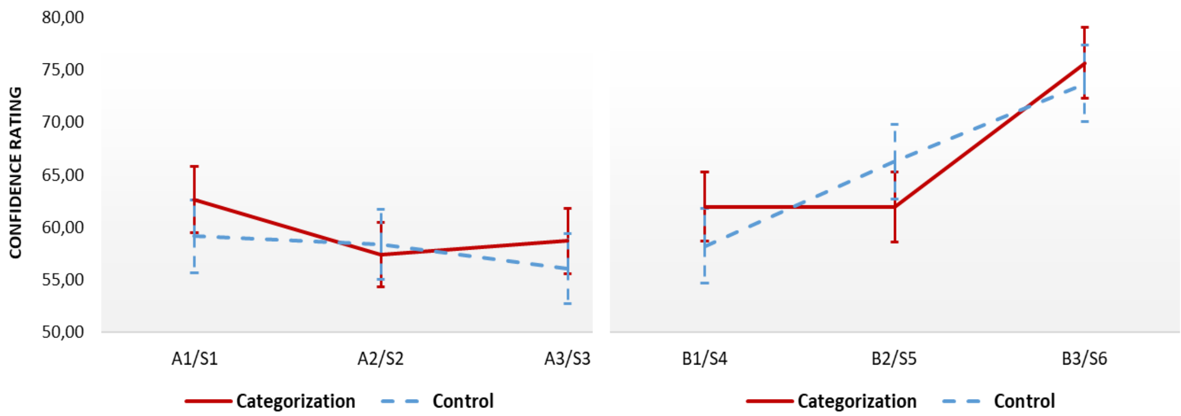

Figure 4. Confidence ratings across groups and stimuli. Error bars are indicative of the standard errors.

3.4 Discussion (STUDY A)

The pain categorization paradigm successfully induced assimilation and accentuation effects across both the learning and recall phases, further supporting the notion that artificial category information can alter pain perception and decision-making processes. Participants in the categorization group reported reduced variability in pain unpleasantness ratings for stimuli within categories relative to stimuli at the category border. The categorization group also showed lower confusion frequencies for stimuli at the category border compared to the control group.

Interestingly, in line with van der Meulen et al.'s results (2017), we found evidence of assimilation and accentuation effects in pain unpleasantness reports, but not in pain intensity. Although correlated, pain intensity and pain unpleasantness are believed to tap into different dimensions of pain experience (i.e., the sensory-discriminative and affective-motivational components of pain respectively; Auvray at el., 2010).

Categorization effects in visual, auditory and tactile perception have predominantly been investigated using sensory stimuli that carry little affective valence or self-relevance. However, our findings raise the interesting possibility that categorization-induced biases may be even more pronounced within the affective domain (although it is important to note that Petersen et al. (2014) did observe modulation of both intensity and unpleasantness reports with aversive respiratory stimuli). Whether this pattern of findings pertains specifically to the nociceptive realm or not remains an intriguing question to be addressed.

Pain ratings, however, do not allow us to disentangle perceptual from decision-making processes i.e., differences in pain ratings may have been the result of the modulatory influence of the categorical information at the perceptual level or instead a post-hoc re-interpretation of stimulus intensity and unpleasantness based on the category information provided during the learning phase. The stimulus identification approach used in the recall phase helps to overcome this issue. During this phase, the heat stimuli were presented without any categorical information and participants were required to correctly identify their corresponding labels. Results from the recall phase largely confirmed the effects observed in the learning phase. We again observed a trend of higher confusion frequencies (i.e., increased perceived similarity) within categories and lower confusion frequencies (i.e., reduced perceived similarity) at the category border in the categorization group, with the opposite trend being observed in the control group. These findings cannot be explained by a simple post-hoc re-anchoring of self-report in line with prior categorical information. Instead, our results suggest that categorization can already exert its modulatory influence at the perceptual level. This interpretation is consistent with growing neuroscientific evidence showing that prior information can modulate sensory processing even at the lower levels of the perceptual hierarchy (de Lange et al., 2018).

Overall, we successfully replicated van der Meulen et al.'s (2017) findings that categorical information can bias both pain perception and decision-making processes. The finding that simple abstract category labels can successfully induce pain-related perceptual biases raises the important question of whether the magnitude of these effects can be modulated via specific cognitive strategies, individual differences, or other psychological factors.

To do so we conducted a follow-up study in which we administered the categorization condition from Study 1 to two groups of participants who differed in their trait mindfulness level. Recent neuroimaging studies (e.g., Gard et al., 2011; Grant et al., 2011), behavioural evidence (e.g., Jha et al., 2007; Kerr et al., 2011) and theoretical models (e.g., Farb et al., 2015; Pagnoni & Porro, 2014) alike all suggest that mindfulness may be accompanied by a prioritization of current sensory input at the expense of prior beliefs or expectations. This hence raises the possibility that (prior) category information may have a reduced influence on pain perception in highly mindful individuals.

Interestingly, conceptualisations of mindfulness steeped in early Buddhist traditions suggest that mindfulness practice can engender a potential uncoupling of the sensory and affective dimensions of pain (Ṭhānissaro Bhikkhu, 1997). Accordingly, some contemporary studies have lent some support to this proposal with observations that mindfulness practice was associated with reduced pain unpleasantness, but not pain intensity, reports (e.g., Perlman et al., 2011; Zorn et al., 2020). Given the differential patterns observed for pain unpleasantness and pain intensity ratings in both the current study and in van der Meulen et al.'s (2017) study, mindfulness constitutes a particularly promising candidate for exploring potential individual differences in susceptibility to categorization-induced biases.

In addition, we also included self-report measures of potential mediating factors (i.e., intolerance of uncertainty, trait and state pain catastrophizing and state mindfulness) that have previously been linked to both mindfulness and expectancy-driven pain modulation (e.g., Morriss et al., 2021; Taylor et al., 2017; Vencatachellum et al., 2021).

Overall, we hypothesized that high trait mindfulness individuals would show reduced assimilation and accentuation effects during both the learning and recall phases, compared to low trait mindfulness individuals.

3.5 Methods (STUDY B)

3.5.1 Participants

Participants were selected from an initial sample of 155 participants who filled in an online questionnaire assessing trait mindfulness levels (i.e., Five Facet Mindfulness Questionnaire; FFMQ). The upper and lower quartiles of FFMQ scorers were invited to take part in the experimental session. Thirty-seven high trait mindfulness (HTM) and 37 low trait mindfulness (LTM) scorers completed the study (mean age = 23.22, SD = 3.93; 62.20% female). They all met the eligibility criteria for participation (the same as in Study 2(a)). None of the participants had significant prior experience with mindfulness practice. Participants were remunerated either via course credits or 15€ worth of gift vouchers.

In addition, participants were also invited to take part in a separate pain conditioning study three to ten days after the pain categorization session (results from the pain conditioning study are reported in Study 3). The experimental protocol was approved by the ethics committee of the University of Luxembourg (ref: ERP 20-007).

3.5.2 Pain categorization paradigm

The pain categorization paradigm was similar to the one used in Study 2(a) with some minor modifications. As the aim of Study 2(b) was to investigate the susceptibility of the HTM and LTM groups to categorization effects, both groups were administered the categorization condition from Study 2(a) (i.e., the six stimuli were labelled A1, A2, A3, B1, B2 and B3 for both groups). The control stimuli from Study 2(a) (i.e., S1-S6) were not used in Study 2(b).

In addition, the learning phase and recall phases both consisted of 36 trials each (six trials per stimulus). Finally, we used a 7-point Likert scale (ranging from 0 = "not confident at all" to 7 = "extremely confident") to assess participants' levels of confidence in their responses during the recall phase.

3.5.3 Self-report questionnaires

Five Facet Mindfulness Questionnaire (FFMQ)

The Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006) was administered as part of an online survey aiming to assess trait mindfulness levels. The questionnaire consists of 39 items (e.g., "I watch my feelings without getting lost in them") rated on a 5-point Likert scale, ranging from 1 (never or very rarely true) to 5 (always true). We summed up the items to compute a total FFMQ score, with higher scores indicative of higher trait mindfulness levels (Cronbach's α for the online survey sample = .91).The mean FFMQ score in our participant recruitment survey (M = 136.51, SD = 18.15) is in line with previously reported score distributions (M = ranging from 126.30 to 137.52, SD = ranging from 13.80 to 19.41) from large-scale studies involving healthy non-meditating samples (Baer et al., 2008; Baer et al., 2011; Van Dam et al., 2009; Goldberg et al., 2016). The lower and upper quartile of FFMQ scorers from the initial recruitment survey were invited to take part in the experimental session.

Intolerance of Uncertainty

The Intolerance of Uncertainty Scale – Short Form (IUS-12; Carleton et al., 2007) was used to assess participants' response style to uncertain, ambiguous, and future situations. The 12 items (e.g., "Unforeseen events upset me greatly") are rated on a 5-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (extremely characteristic of me). We computed an overall mean IUS-12 score, with higher scores indicative of higher intolerance of uncertainty levels (Cronbach's α in the current sample = .87).

Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS; Sullivan et al., 1995) was used to assess participants' tendency to engage in catastrophic thinking about current and future pain. The questionnaire consists of 13 items (e.g., ""There is nothing I can do to reduce the intensity of the pain"), rated on a 5-point Likert scale, ranging from 0 (not at all characteristic of me) to 4 (entirely characteristic of me). We computed an overall mean PCS score, with higher scores indicative of higher trait pain catastrophizing levels (Cronbach's α in the current sample = .89).

Toronto Mindfulness Scale

The Toronto Mindfulness Scale (TMS; Lau et al., 2006) was used as a retrospective measure of participants' mindfulness levels during the pain categorization task. The scale consists of 13 items (e.g., "I was more concerned with being open to my experiences than controlling or changing them"), rated on a 5-point Likert scale, ranging from 0 (not at all) to 4 (very much). We computed an overall mean TMS score, with higher scores indicating higher state mindfulness levels (Cronbach's α in the current sample = .81).

Mindful Attention Awareness Scale

The state version of the Mindful Attention Awareness Scale (MAAS; Brown & Ryan, 2003) was used as an additional state mindfulness measure (with a particular focus on levels of mindful attention during the pain categorization task). The scale consists of 5 items (e.g., "I was preoccupied with the future or the past"), rated on a 7-point Likert scale, ranging from 0 (not at all) to 6 (very much). Items were reversed scored and averaged to compute a mean MAAS score, with higher scores indicative of higher mindful attention levels (Cronbach's α in the current sample = .77).

Situational Pain Catastrophizing Scale

The Situational Catastrophizing Scale (SCS; Campbell et al., 2010) was administered as a retrospective measure to assess levels of catastrophic thinking during the pain categorization task. The questionnaire consists of 6 items (e.g., "I couldn't stop thinking about how much it hurt"), rated on a 5-point Likert scale, ranging from 0 (not at all) to 4 (all the time). We computed an overall mean SCS score, with higher scores indicative of higher state pain catastrophizing levels (Cronbach's α in the current sample = .73).

3.5.4 Procedure

Participants provided informed consent and filled in the IUS and PCS questionnaires at the start of the session. We first conducted the pain calibration to derive individual temperatures for the six stimuli. Participants then completed the learning and recall phase of the pain categorization paradigm, with a self-timed break in-between. Finally, they filled in the TMS, MAAS and SCS questionnaires.

3.5.5 Data analysis

We again computed intra-individual variability in pain intensity and unpleasantness ratings for the learning phase, and confusion frequencies (i.e., generalization index 'g') for the recall phase. Similar to Study 2(a), we conducted separate two-way ANOVAs on the intra-individual variability scores, confusion frequencies and confidence ratings, with the difference that the Group factor comprised the HTM and LTM groups (as opposed to the categorization vs. control contrast).

We also conducted independent samples t-tests to probe potential group differences in PCS, IUS, TMS, MAAS and SCS scores. As these analyses revealed significant group differences in some of these measures (see results section), we repeated the aforementioned two-way ANOVAs with the self-report measures included as covariates. However, these ANCOVAs did not alter the pattern of results. Therefore, we only report the initial two-way ANOVAs in the results section below.

3.6. Results (STUDY B)

3.6.1 Group characteristics

The HTM (72% female, 28% male) and LTM (53% female, 47% male) groups differed marginally, but not significantly, in terms of gender distribution, ($\chi 2(1, N = 72) = 2.90$ p = .09). The two groups did not differ on age ($F(1, 70) = 2.61$, $p = .11$) and on the stimuli temperatures used during the pain categorization task ($F(1,70) = .01$, $p = .91$).The HTM group had significantly higher FFMQ scores ($t(70) = 20.97$, $p < .001$) and lower intolerance of uncertainty levels ($t(70) = -4.19$, $p < .001$) than the LTM group. The two groups did not differ on PCS scores, $t(70) = 1.63$, $p = .11$.

Table 3. Mean (SD) and F values for trait and state measures.

	HTM (*N* = 37)	LTM (*N* = 37)	*t*(1, 70)
Trait measures			
FFMQ (39 - 195)	156.41 (8.60)	116.68 (7.56)	20.97***
IUS-12 (1 - 5)	2.40 (0.77)	3.05 (0.53)	- 4.19***
PCS (0 - 4)	2.53 (0.67)	2.80 (0.71)	- 1.63
State measures			
SCS (0 - 4)	0.54 (0.46)	0.84 (0.63)	- 2.33*
TMS (0 - 4)	2.56 (0.73)	2.18 (0.48)	2.58*
MAAS (1 - 6)	4.84 (0.94)	3.92 (1.22)	3.60***

FFMQ (Five Facet Mindfulness Questionnaire), IUS-12 (Intolerance of Uncertainty – Short Form), PCS (Pain Catastrophizing Scale), SCS (Situational Catastrophizing Scale), TMS (Toronto Mindfulness Scale), MAAS (Mindful Attention Awareness Scale); scale ranges are provided alongside each measure. Note: *** = $p < .001$, ** = $p < .01$, * = $p < .05$.

3.6.2 Confusion frequencies

Pain intensity and unpleasantness ratings

The two (Group) x six (Stimuli) mixed ANOVA conducted on the pain intensity ratings revealed a significant main effect of Stimuli (F(1.62,113.07) = 318.50, p < .001, η_p^2 = .79), but no significant Group effect (F(1,70) = 0.44, p = .51, η_p^2 = .01) or Group x Stimuli interaction effect (F(1.62,113.07) = 0.31, p = .69, η_p^2 = .004). Follow-up pairwise comparisons confirmed that there were significant differences in intensity ratings between each adjacent pair of stimuli, t(71)'s ranging from 10.11 to 14.70, p's all < .001.

A similar analysis conducted on the pain unpleasantness ratings again revealed a significant main effect of Stimuli (F(1.73,121.28) = 258.32, p < .001, η_p^2 = .79), but no significant Group effect (F(1,70) = 0.83, p = .37, η_p^2 = .01) or Group x Stimuli interaction effect (F(1.73,121.28) = 0.45, p = .94, η_p^2 = .001). The follow-up pairwise comparisons showed that each adjacent pair of stimuli differed significantly in pain unpleasantness ratings, t(71)'s ranging from 8.26 to 9.50, p's all < .001.

These analyses confirmed that participants successfully detected the increase in temperatures across stimuli. Pain intensity and unpleasantness ratings across groups and stimuli are depicted in Tables 4 and 5.

Table 4. Mean (SD) and *t* values for pain intensity ratings.

	Pain Intensity					
	A1	A2	A3	B1	B2	B3
LTM	31.44 (15.90)	37.99 (12.70)	45.96 (11.03)	56.01 (10.98)	64.69 (101.10)	73.06 (11.71)
HTM	28.31 (13.96)	36.68 (12.29)	44.95 (11.19)	54.13 (9.69)	63.09 (10.63)	73.02 (11.51)
t(70)	0.89	0.45	0.38	0.77	0.65	0.02

Table 5. Mean (SD) and *t* values for pain unpleasantness ratings.

	Pain Unpleasantness					
	A1	A2	A3	B1	B2	B3
LTM	22.26	30.19	37.81	48.21	58.16	66.34
	(16.43)	(13.36)	(11.82)	(12.13)	(11.29)	(12.47)
HTM	19.70	27.24	35.89	46.07	55.44	64.47
	(14.93)	(14.85)	(14.23)	(13.98)	(13.27)	(14.66)
t(70)	0.69	0.89	0.62	0.69	0.94	0.58

Intra-individual variability in pain ratings

The two-way ANOVA conducted on the computed intra-individual variability in pain intensity ratings revealed a significant main effect of category ($F(1.62,113.51) = 4.41$, $p = .01$, $\eta_p^2 = .06$) but no effect of Group ($F(1,70) = 0.32$, $p = .58$, $\eta_p^2 = .004$). Follow-up pairwise comparisons showed higher variability scores for stimuli at the category border (SD_{AB}) relative to stimuli within Category A (SD_A), $t(71) = 2.67$, $p = .03$. The other pairwise comparisons were not significant (*p*'s all > .10). The quadratic Group x Category interaction effect was not significant ($F(1,70) = 0.26$, $p = .61$, $\eta_p^2 = .004$).

The two-way ANOVA conducted on the computed intra-individual variability in pain unpleasantness ratings again revealed a significant main effect of category ($F(1.64,114.75) = 5.34$, $p = .01$, $\eta_p^2 = .07$) but no effect of Group ($F(1,70) = 0.23$, $p = .63$, $\eta_p^2 = .003$). Follow-up pairwise comparisons showed higher SD_{AB} scores relative to SD_A) ($t(71) = 2.82$, $p = .02$), with no other significant comparisons (*p*'s all > .10). We also failed to observe any quadratic Group x Category interaction effect ($F(1,70) = 0.17$, $p = .68$, $\eta_p^2 = .002$). Intra-individual variability for pain intensity and pain unpleasantness ratings are depicted in Figure 5.

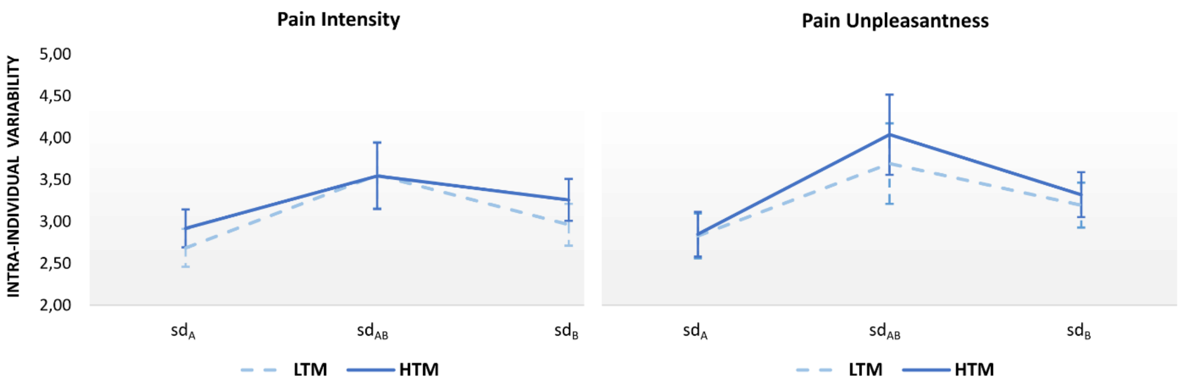

Figure 5. Intra-individual variability in pain intensity and unpleasantness ratings across groups and categories. Error bars are indicative of the standard errors.

Confusion frequencies

The two-way ANOVA conducted on the computed confusion frequencies revealed no significant effects of Group (F(1,70) = 0.15, p = .70, η_p^2 = .002) or Category (F(2,140) = 0.25, p = .78, η_p^2 = .003). We also failed to observe any quadratic Group x Category interaction effect, F(1,70) = 0.48, p = .49, η_p^2 = . 01. Although visual inspection of Figure 6 appears to hint at the hypothesized trend of higher confusion frequencies for g_A in the LTM group relative to the HTM group, the post-hoc pairwise comparison failed to reach significance, t(70) = 1.66, p = .10 (*Cohen's d* was a small to moderate effect size of .38). The other pairwise comparisons were also not significant, p's all > .10. Confusion frequencies across groups and categories are depicted in Figure 6.

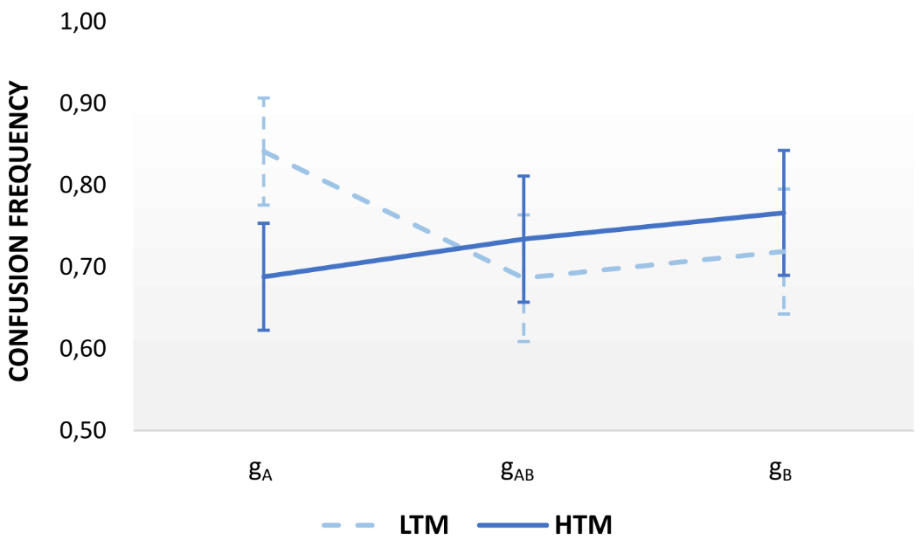

Figure 6. Confusion frequencies across groups and categories. Error bars are indicative of the standard errors.

Confidence ratings

The two-way ANOVA conducted on confidence ratings for stimuli in Category A revealed a significant effect of Stimulus (F(2,140) = 26.00, p < .001, η_p^2 = .06) but not of Group (F(1,70) = 0.02, p = .89, η_p^2 = . 00). Follow-up pairwise comparisons revealed that confidence ratings for stimulus A2 was significantly lower than for A1 (t(71) = -3.79, p < .001) but significantly higher than for A3 (t(71) = 3.94, p < .001). We found no Group x Stimulus interaction effect, F(2,140) = 0.26, p = .77, η_p^2 = .004.

The two-way ANOVA conducted on confidence ratings for stimuli in Category B again revealed a significant effect of Stimulus (F(1.72,120.31) = 39.70, p < .001, η_p^2 = . 36) but not of Group (F(1,70) = 0.02, p = .88, η_p^2 = . 00). Follow-up pairwise comparisons revealed that confidence ratings for stimulus B2 were significantly higher than for B1 (t(71) = 3.32, p < .01) but significantly lower than for B3 (t(71) = -6.30, p < .001). We found no Group x Stimulus interaction effect, F(1.72,120.31) = 1.08, p = .34, η_p^2 = . 02. Confidence ratings across groups and categories are depicted in Figure 7.

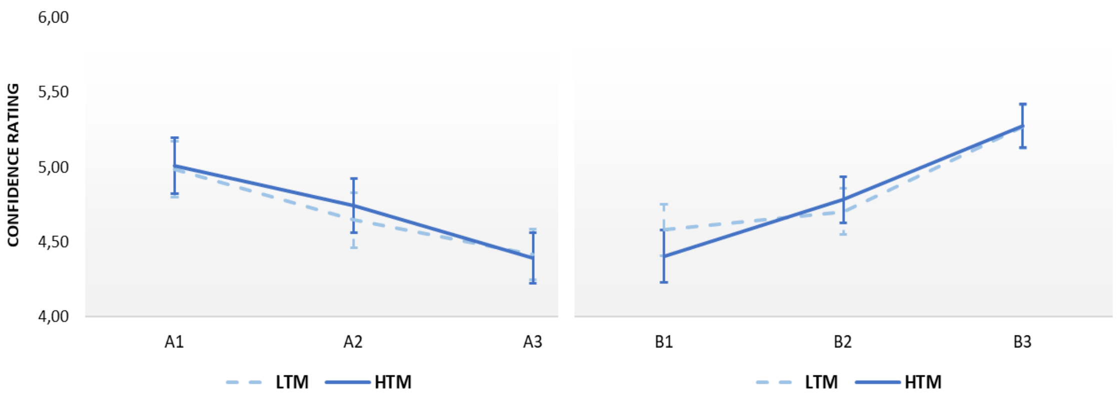

Figure 7. Confidence ratings across groups and stimuli. Error bars are indicative of the standard errors.

3.7 Discussion (STUDY B)

In Study 2(b), we tested whether the magnitudes of the categorization-induced perceptual biases observed in Study 2(a) could be modulated by trait mindfulness level. In line with previous evidence that mindfulness can reduce sensitivity to conditioning procedures (Taylor et al., 2018; Vencatachellum et al., 2021)), we hypothesized that individuals high in trait mindfulness levels would show similar reduced susceptibility to the categorization manipulation. However, contrary to our predictions, we found no differences in assimilation and accentuation effects in pain intensity and unpleasantness reports between the HTM and LTM groups during the learning phase. Likewise, although visual depiction of our results hinted at the hypothesized trend for computed confusion frequencies, subsequent analyses failed to reveal any significant group differences. Trait mindfulness level also failed to modulate the influence of the category labels on confidence reports.

It is important to mention at this juncture that Study 2(b) did not consist of a control (i.e., no-categorization) condition. Therefore, it cannot be fully ruled out that Study 2(b) failed to replicate the categorical biases induced in Study 2(a), which would therefore explain the lack of mindfulness-related modulation. However, we deem this unlikely as the pattern of responses in both the HTM and LTM groups closely mirrored that observed for the categorization group in Study 2(a). Instead, we would posit that the disparate findings between our pain categorization study and previous pain conditioning studies are more likely due to differences in underlying neuropsychological mechanisms or methodological choices across these studies. One possibility is that prior categorical information may affect pain perception at a different processing stage compared to the cued information used in conditioning paradigms. The lack of modulation in the current study raises the possibility that categorization processes may occur at a more fundamental level, which may render them more resistant to top-down modulation, although this claim would need to be confirmed by further research. Another potential explanation for the lack of modulation may be due to the smaller effect sizes typically reported for categorization effects, relative to conditioning effects. It is thus also important to highlight the methodological differences between the categorization and conditioning paradigms. Firstly, our pain categorization paradigm comprised a greater number of (labelled) stimuli than is typically included in conditioning paradigms (e.g., two cued stimuli in both Taylor et al. (2018) and Vencatachellum et al. (2021)). Secondly, there is usually a clearer demarcation in temperature range between stimuli in the conditioning paradigm than the 0.5°C increments between our stimuli in the current study. Altogether, these factors may contribute to making it considerably harder to identify, learn and memorize the label-stimulus associations in the categorization paradigm, thereby explaining the smaller effect sizes reported in such paradigms. Finally, the pain categorization paradigm does not include any manipulation of label-stimulus contingencies or any form of deception. Contrary to conditioning paradigms whereby cue-stimulus contingencies are usually manipulated, unbeknownst to the participant, between the learning and testing phase, label-stimulus contingencies are left unchanged across the learning and recall phases of the pain categorization paradigm. It must also be noted that Taylor et al. (2018) found evidence of reduced fear-conditioned pain modulation in experienced meditators relative to non-meditators while we found reduced conditioned hypoalgesic effects following a brief mindfulness induction relative to a suppression condition. It is thus possible that the disparate findings could be due to the different ways mindfulness was operationalized across these three studies (although it must be noted that we did observe evidence of reduced conditioned hyperalgesia in the HTM group in a follow-up pain-cueing study with the same sample of participants; findings are reported in detailed in empirical Study 3).

Notwithstanding the above considerations, our findings overall suggest that participants may be susceptible to categorization-induced perceptual biases, regardless of their trait mindfulness level. Given that mindfulness has previously been linked with increased pain tolerance, improved pain symptomology, reduced conditioned hyperalgesia and lower pain catastrophizing ((Hilton et al., 2016; Lakhan & Schofield, 2013; Veehof et al., 2011, 2016).), the apparent pervasiveness of categorization-induced biases bears important clinical implications. The finding that categorical information can facilitate confusion of stimuli falling under similar category labels is of particular relevance, as poorer differentiation of sensations is susceptible to increase the likelihood of pain-related fear generalization and maladaptive or rigid coping behaviours (both common factors in the aetiology and maintenance of chronic pain (Di Lernia et al., 2016). Yet, patients are often queried about their symptoms using categorical pain labels during medical consultations. Our findings highlight potential issues with this approach for diagnostic purposes. A move from categorical labels to a more dimensional approach (e.g., presenting and querying about sensations on a continuous spectrum) may help preserve the granularity of sensory information and reduce the aforementioned biases. Such a de-categorization approach has previously been shown to reduce intergroup bias in social categorization studies (Gaertner, Mann, Murrell, & Dovidio, 1989).

3.8 Conclusion

Our study provides important supporting evidence for the notion that mere abstract category labels can bias pain perception. Pain categorization research is, however, still in its infancy and key questions remain to be addressed. We conclude by highlighting some potential avenues for furthering this line of research. First, it would be important to establish the neural mechanisms of pain categorization biases and whether these differ from other forms of expectancy-driven pain modulation. For instance, effective connectivity studies have already begun to unravel the neural pathways involved in placebo analgesia (Sevel et al., 2015). Likewise, disentangling the different cognitive processing stages involved in pain categorization is also likely to offer important additional insight. Event-related potentials that have been observed in other pain modulation paradigms (e.g., cue-evoked potential, stimulus preceding negativity, stimulus evoked response) may help delineate the relative contribution of prior information, anticipatory and sensory processes on perceptual and decision-making outcomes. It would also be important to determine whether the null findings between our two groups also extend to comparisons between experienced vs novice meditators, pre- vs. post-mindfulness training and mindfulness induction vs. other forms of cognitive pain modulation. Furthermore, we hypothesized that trait mindfulness would be associated with reduced categorization-induced biases on the assumption that mindful attention prioritizes current sensory input over prior expectations. An alternative approach would be to directly compare accurate vs. non-accurate pain reporters (e.g., via the Focused Analgesia Selection Test; Treister et al., 2017). We may expect that individuals with higher pain reporting precision (i.e., reduced variability in ratings across identical stimuli) would show reduced susceptibility to categorization procedures. Using this approach, Treister et al. (2019) recently demonstrated a similar link between variability in reported pain and the placebo response. Finally, while we successfully probed the biasing influence of category labels on both pain perception and decision-making processes, it would be important for future research to also ascertain how pain-related category information shape behavioural coping responses. For instance, Petersen et al. (2014) previously showed that, in addition to the modulation of perceptual and identification outcomes, categorization can also significantly alter breathing behaviour (assessed via changes in inspiratory flow).

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4 STUDY III: Reduced Vulnerability to Conditioned Hyperalgesia in Highly Mindful Individuals

4.1 Abstract

Novel neuroimaging evidence suggest that mindfulness-induced pain alleviation may be driven by increased activation of sensory processing areas and concomitant decreased activation of evaluative and memory-related regions. In light of these observations, recent predictive processing models opine that mindfulness may mitigate the well-documented biasing influence of expectations on perception. We tested this hypothesis using an explicit classical pain conditioning paradigm. 36 high (HTM) and 32 low (LTM) trait mindfulness scorers took part in a pain cueing task, during which they first learned to associate a high and a low pain cue with high and low pain heat stimuli respectively. They then took part in a testing phase whereby they rated pain intensity and unpleasantness of identical heat stimuli, which were preceded by either the low pain cue, the high pain cue or a novel cue. The HTM group reported lower overall pain intensity and pain unpleasantness ratings. Importantly, the HTM group showed reduced conditioned hyperalgesic effects in pain unpleasantness compared to the LTM group. There were no group differences in conditioned hypoalgesia. We also observed positive associations between pain catastrophizing, intolerance of uncertainty and conditioned hyperalgesia. The results provide partial support for recent predictive processing models of mindfulness which posit that mindfulness may lead to the prioritisation of afferent sensory information over prior expectations. Our findings also suggest that mindfulness cultivation may provide a potential pathway to countering the hyperalgesic effects of pain catastrophizing and intolerance of uncertainty.

4.2 Introduction

The influence of prior pain-related expectations and information on the subjective experience of pain has been vastly documented within the research literature (Atlas & Wager, 2012). Accordingly, identifying potential predictors of expectancy-driven perceptual biases has been the object of increasing scientific attention in recent years (Kong & Benedetti, 2014; Testa & Rossettini, 2016). Of particular clinical relevance are recent findings indicating that similar neuropsychological factors and mechanisms may be involved in both the amplification of expectancy-driven hyperalgesia and the chronification of pain (Blasini et al., 2017; Corsi & Colloca, 2017; Thomaidou et al., 2021). It is therefore equally essential to identify factors and strategies that may help in countering the biasing influence of expectations on pain experience.

Recent insights from neuroimaging investigations of mindfulness-driven pain modulation suggest that mindfulness may provide a potentially promising pathway towards countering these biases. These studies have typically shown that pain attenuation in experienced mindfulness meditators is associated with increased neural activation of sensory processing regions and a concomitant decrease in activation of putatively cognitive-evaluative and memory-related processing regions (Gard et al., 2011; Grant et al.; 2011; Lutz et al.; 2013). This activation pattern has been interpreted as reflective of the non-elaborative and non-evaluative monitoring of arising sensory and cognitive stimuli prescribed by mindfulness practice. On the basis of these observations, recently formulated mechanistic accounts of mindfulness opined that mindfulness may promote perceptual objectivity (i.e., enhanced sensory processing) by mitigating the influence of prior beliefs and expectations (i.e., abatement of memory-related processing) on (pain) perception (Farb et al., 2015; Pagnoni and Porro, 2014).

Taylor et al. (2018) recently provided an initial test of this possibility. Using a classical fear-conditioning paradigm, they observed that experienced meditators with over 1,000 hours of mindfulness practice exhibited reduced conditioned hyperalgesic effects compared to meditation-naïve controls. Interestingly, meditators did not differ from controls in terms of learning processes (as evidenced by preserved discriminative anticipatory skin conductance responses), suggesting that mindfulness practice may mitigate the influence of pain-related expectations on perception while maintaining awareness of cue-stimulus associations. Nevertheless, Taylor et al.'s study focused exclusively on the impact of extensive meditation experience on the hyperalgesic effects of pain expectation. If, as the aforementioned theoretical interpretations of current neuroimaging evidence suggest, mindfulness does lead to an attenuated influence of previous beliefs, expectations and information on pain perception, then we may also expect to observe similar mindfulness-induced modulation of expectancy-induced hypoalgesia.

Accordingly, we recently investigated the modulatory influence of brief mindfulness training on both conditioned hypoalgesic and hyperalgesic effects (Vencatachellum et al., 2021). Specifically, we tested whether instructed use of a mindfulness vs. an alternative cognitive regulatory strategy (i.e., suppression) differentially modulates the magnitudes of conditioned hypoalgesia and hyperalgesia during a classical pain-cueing paradigm. Although the paradigm was successful in eliciting both cue-induced hypoalgesia and hyperalgesia, we only found partial support for the notion that mindfulness reduces susceptibility to pain conditioning procedures. In support of our hypothesis, our results indicated that while participants in the suppression condition showed evidence of cue-induced hypoalgesic effects, no such effects were found for participants instructed in the use of the mindfulness strategy. Notably, the mindfulness group reported lower, albeit non-significant, pain ratings on unconditioned trials compared to the suppression group. Likewise, the two groups did not differ on cue-stimulus contingency awareness checks. These findings thus suggest that the absence of conditioned hypoalgesia in the mindfulness group was likely driven by a mitigation of the impact of the prior cue-stimulus contingency information on pain perception, and not the result of weaker pain alleviation or poorer learning processes.

However, contrary to our predictions, we failed to observe any group differences with regards to cue-induced hyperalgesic effects. We speculated that the explanation for the asymmetric patterns observed for conditioned hypoalgesic vs. hyperalgesic effects may reside in their differential resistance to modulation. From an adaptive perspective, ignoring information about imminent threat can result in potentially deleterious consequences. As such, information signalling an upcoming painful event (e.g., a conditioned high pain cue) is likely to be afforded higher weight in perceptual and decision-making processes, relative to a conditioned low pain cue. In support of this explanation, previous comparisons of conditioned nocebo and placebo effects have found nocebo effects to be significantly more resistant to extinction (Colagiuri et al., 2015; Colloca et al., 2008).

Moreover, given the brevity of our mindfulness training condition, these findings are limited in their generalizability to other operationalisations of mindfulness. For instance, previous neuroimaging studies have reported that brief mindfulness training may elicit slightly different patterns of neural activation during pain stimulation to those observed in experienced meditators (Zeidan et al., 2019). Furthermore, participants in our mindfulness condition scored higher than the suppression group on the decentering subscale of a state mindfulness questionnaire (Toronto Mindfulness Scale; Lau et al., 2006), but not on the curiosity subscale or the aggregated state mindfulness score, further suggesting that our brief mindfulness induction may have been limited in its modulatory power. As demonstrated by Taylor et al.'s findings, we can therefore not rule out that experienced meditators (or highly mindful individuals) may still exhibit the hypothesised reductions in conditioned hyperalgesic effects.

Finally, interpretation of our results was limited by the fact that our mindfulness condition was contrasted against the instructed use of a suppression strategy. We opted to use a suppression condition as our comparison group; (i) as suppression instructions (i.e. aiming to inhibit/reject/block out arising sensations and feelings) provide a sharp contrast to the accepting, non-judgmental stance encouraged by the mindfulness instructions, and (ii) in order to reduce potential heterogeneity in coping strategies used by participants during pain stimulation (as is likely to be the case in a no-instructions control condition; Van Ryckeghem et al., 2018). However, this approach does not allow us to conclusively determine the extent to which the observed group differences were driven purely by the hypothesized mindfulness-induced reductions in expectancy-related biases. In other words, we could not rule out the possibility that these observations may have instead resulted from an amplification of conditioned hypoalgesic effects by the suppression instructions.

In the current study, we aimed to address these methodological limitations by comparing high trait mindfulness and low trait mindfulness individuals in their sensitivity to both conditioned hypoalgesic and hyperalgesic effects during an explicit classical pain-cueing paradigm. Recent neuroimaging evidence suggests that lower pain reports in high trait mindfulness individuals may be achieved by similar neural mechanisms to those reported in neuroimaging studies of expert meditators (Harrison et al., 2019; Zeidan et al., 2018).

Overall, we first expected to replicate our previous findings that mindfulness is associated with reduced conditioned hypoalgesic effects (Vencatachellum et al., 2021). Furthermore, in line with Taylor et al. (2018), we also hypothesized that individuals scoring high in trait mindfulness levels would exhibit reduced conditioned hyperalgesic effects compared to low trait mindfulness scorers.

4.2 Methods

4.2.1 Participants

Participants for the experimental session were selected from an initial sample of 155 participants, who filled in an online survey assessing trait mindfulness levels (via the Five Facet Mindfulness Questionnaire - FFMQ; Baer et al., 2006). The survey was advertised via flyers and on a University's webpage dedicated to participant recruitment. The study was described as investigating potential psychological factors which may influence pain perception and anxiety. The upper and lower quartiles of FFMQ scorers were invited to take part in both Study 2(b) and the present study. There was a gap of 3 to 10 days between the two experimental sessions. In addition, a screening procedure was conducted to ensure that invited participants did not suffer from acute or chronic pain, mental conditions or neurological diagnoses (anxiety, depression, post-traumatic stress disorder, schizophrenia, substance abuse, dementia, epilepsy, stroke or Parkinson's disease) and were not taking any medication with potential pain modulatory effects. A final sample of 36 participants high in trait mindfulness (HTM) and 32 participants low in trait mindfulness scores (LTM) attended the experimental session (overall mean age = 23.07, SD = 3.82; 63.2% female). None of the participants had significant prior experience with mindfulness practice. Participants provided written informed consent prior to participation and were remunerated via course credit or gift vouchers at the end of the session. The experimental protocol was approved by the ethics committee of the University of Luxembourg (ref: ERP 20-007).

4.2.2 Pain-cueing task

The pain-cueing task consisted of an acquisition phase and a testing phase. In the acquisition phase, a blue visual cue (i.e., low pain cue) was systematically followed by the low pain stimulus while a red visual cue (i.e., high pain cue) preceded the high pain stimulus. Participants were explicitly informed prior to the pain cueing task that the blue cue was predictive of a low heat stimulus and that the red cue was predictive of a high heat stimulus. The visual cues were in the shape of combined bullseye and cross hair (as used by Thaler et al., 2013). The cue was presented for a duration ranging from 8 to 10 seconds, followed by delivery of the heat stimulus for 7 seconds. At the end of each trial, participants were asked to rate the levels of anticipatory anxiety, pain intensity and pain unpleasantness that they experienced during the trial. The acquisition phase comprised two blocks of 10 trials (i.e., five of each cue type per block), with an inter-trial interval of 10 seconds. The trials were presented in a fixed random order (see Figure 1(a)).

The testing phase comprised a series of conditioned trials (identical to the acquisition phase) and test trials. In contrast to the conditioned trials, all heat stimuli during the test trials were delivered at the medium pain temperature (derived from the calibration procedure). These heat stimuli were preceded by either the blue cue, the red cue, or a novel (i.e., grey) visual cue. The testing phase consisted of three blocks of 20 trials each and followed a trial timeline similar to the acquisition phase. Conditioned and test trials were presented in a fixed random order (see Figure 1(b)). Distribution of conditioned and test trials during the acquisition and testing phases are depicted in Figure 1.

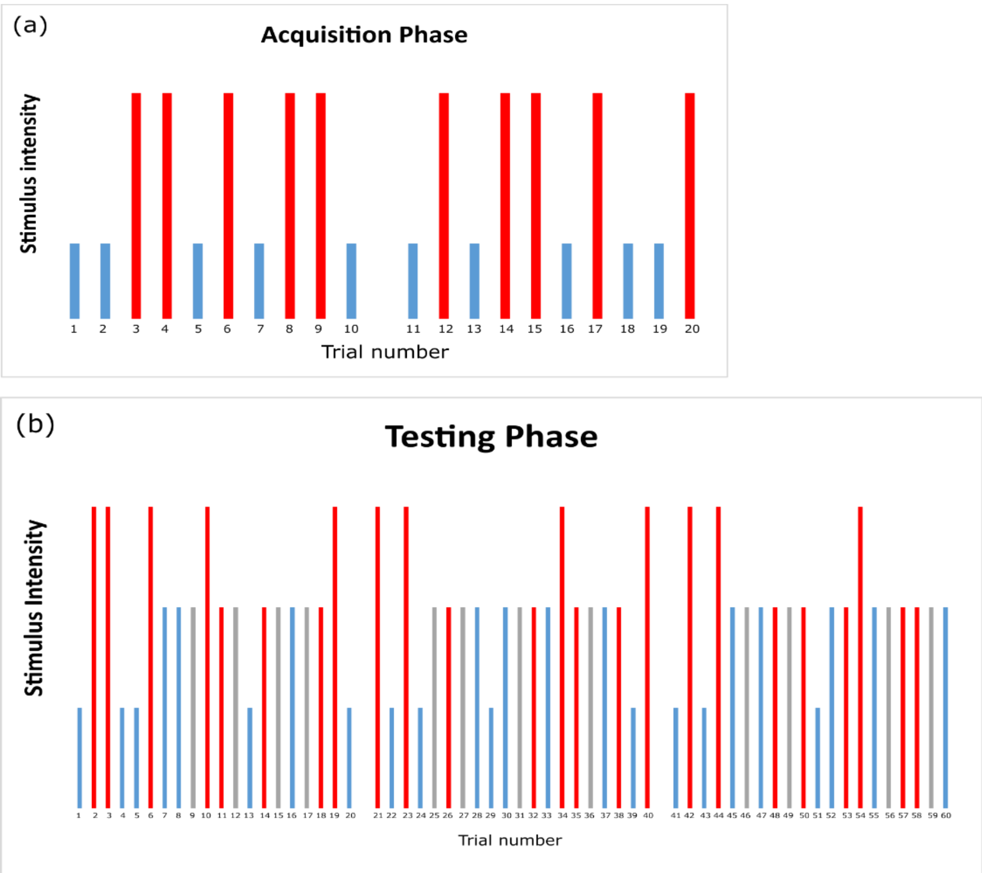

Figure 1. Distribution of conditioned and test trials during the acquisition (a) and testing phases (b).

4.2.3 Thermal pain stimulation

Heat stimuli were administered via a contact thermal stimulator (Somedic AB, Sweden), which was attached to the volar surface of the participant's left forearm. We conducted a pain calibration procedure prior to the pain cueing task to derive individual heat temperatures for each participant. Participants first received a pseudorandomized series of nine heat stimuli, ranging from 43°C to 47°C in increments of 0.5°C. They were asked to indicate on a 100-point VAS (0 = 'No pain' to 100 = 'Unbearable pain') the pain level they experienced for each temperature. We fitted a sigmoid (Weibull) function (Yoshida et al., 2013) to the participant's ratings to derive the temperatures that elicited pain levels of 25 (low pain), 50 (medium pain) and 75 (high pain). We then repeated the procedure a second time adjusting the temperature range for the heat stimuli in accordance with the newly derived temperatures. Each thermal heat stimulus lasted for 7 s (ramp up: 2 s; plateau: 3 s; ramp down: 2 s), with a baseline temperature of 35°C.

4.2.4 Self-report measures

Five Facet Mindfulness Questionnaire

The Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006) is a commonly used measure to assess dispositional mindfulness levels. The questionnaire comprises 39 items (e.g., "I watch my feelings without getting lost in them") rated on a 5-point Likert scale ranging from 1 (never or very rarely true) to 5 (always true). Items were summed up to compute a mean FFMQ score (Cronbach's $\alpha = .91$), with higher scores indicative of higher trait mindfulness levels. Participants for the study were selected on the basis of their FFMQ scores (upper vs. lower quartile). As described in Study 2(b), the FFMQ score distribution in our initial participant selection survey was in line with previously reported score distributions in large-scale healthy non-meditators populations.

Intolerance of Uncertainty

The Intolerance of Uncertainty Scale-12 (IUS-12; Carleton et al., 2007) was used to assess individual reactions to the uncertainty associated with ambiguous or future situations. The IUS-12 is a short form of the original Intolerance of Uncertainty Scale (Freeston et al., 1994), and comprises 12 items (e.g., "Unforeseen events upset me greatly") rated on a 5-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me). Item scores were averaged to compute a mean overall IUS-12 score (Cronbach's α = .87), with higher scores indicating higher intolerance of uncertainty levels.

Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS; Sullivan et al., 1995) is a trait questionnaire which aims to assess an individual's tendency to engage in catastrophic thinking about current and future pain. The questionnaire consists of 13 items (e.g., "There is nothing I can do to reduce the intensity of the pain") rated on a 5-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me). A mean overall PCS score was computed (Cronbach's α = .89), with higher scores indicative of higher trait catastrophizing levels.

Toronto Mindfulness Scale

The Toronto Mindfulness Scale (TMS; Lau et al., 2006) was used as a measure of state mindfulness level. The scale comprises 13 items (e.g., "I was more concerned with being open to my experiences than controlling or changing them") rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much). We computed a mean overall TMS score (Cronbach's α = .84), with higher scores indicative of higher state mindfulness levels.

Mindful Attention Awareness Scale

The state-Mindful Attention Awareness Scale (MAAS; Brown & Ryan, 2003) was used as an additional state mindfulness measure (with a particular focus on assessing participants' level of mindful attention during the pain-cueing task). The questionnaire comprises five items (e.g., "I was preoccupied with the future or the past") rated on a 7-point Likert scale ranging from 0 (not at all) to 6 (very much). Items were reversed scored and averaged to compute a mean MAAS score (Cronbach's α = .86), with higher scores reflective of higher mindful attention levels (i.e., reduced mind wandering) during the pain-cueing task.

Situational Pain Catastrophizing Scale

The Situational Catastrophizing Scale (SCS; Campbell et al., 2010) was used to assess participants' tendency to engage in catastrophic thinking during the pain-cueing task. The questionnaire comprises six items (e.g., "I couldn't stop thinking about how much it hurt"), rated on a 5-point Likert scale, ranging from 0 (not at all) to 4 (all the time). An overall mean SCS score (Cronbach's $\alpha = .83$) was computed, with higher scores indicative of higher state pain catastrophizing scores.

Anticipatory anxiety and pain (VAS) ratings

Participants were asked to rate the levels of anticipatory anxiety (i.e., anxiety level before the delivery of the heat stimulus), pain intensity (i.e., intensity of the heat stimulus) and pain unpleasantness (i.e., aversiveness of the heat stimulus) that they experienced during each trial of the pain-cueing task. They did so via visual analogue scales (VAS), ranging from 0 (not anxious/intense/unpleasant at all) to 100 (extremely anxious/intense/unpleasant). To clarify the distinction between pain intensity and pain unpleasantness to participants, we used verbal instructions that were similar to those used by Price et al. (1983).

4.2.5 Procedure

After providing informed consent, participants were asked to fill in the PCS and IUS-12 questionnaires. They were then seated approximately 80 cm away from a 24-inch screen monitor in a laboratory room dedicated to pain research. Participants used a mouse and keyboard to respond to all VAS scales presented during the experimental session. We first carried out the temperature-pain calibration procedure to derive individual temperatures for the low, medium and high pain levels. Participants then underwent the acquisition phase, followed by the testing phase, of the pain-cueing task. Finally, they filled in the SCS, TMS and MAAS questionnaires. Participants were fully debriefed as to the purpose of the study at the end of the session. We employed a similar data analytic approach to that used Study 1.

4.3 Results

4.3.1 Baseline measures

The two groups did not differ significantly on gender distribution ($\chi^2(1, N = 68) = 2.66$, $p > .10$) or age ($F(1, 66) = 2.30$, $p > .10$). The high trait mindfulness group (HTM) scored significantly higher on trait mindfulness and significantly lower on intolerance of uncertainty and trait pain catastrophizing compared to the low trait mindfulness group (LTM). The two groups did not differ on the pain thresholds derived from the calibration procedure. The HTM group reported significantly lower anticipatory anxiety levels on both low-cued and high-cued trials during the acquisition phase, with no group differences observed in pain intensity and pain unpleasantness ratings. Table 1 summarizes the group means, SDs and statistics for the baseline measures.

Table 1. Mean (SD) and F values for baseline measures.

	HTM (N = 36)	LTM (N = 32)	F(1, 66)
FFMQ (39 - 195)	157.36 (9.27)	116.50 (7.86)	379.11***
IUS-12 (1 - 5)	2.40 (0.76)	3.07 (0.51)	16.46***
PCS (0 - 4)	2.47 (0.62)	2.88 (0.67)	6.31*
Pain thresholds (°C)			
Low	45.24 (1.35)	45.25 (1.24)	0.00
Medium	46.82 (1.16)	46.89 (1.05)	0.07
High	48.28 (1.07)	48.34 (0.97)	0.07
Acquisition Phase			
Low-cued ratings (0 – 100)			
Anticipatory Anxiety	11,09 (10.30)	18.84 (12.69)	7.60**
Pain Intensity	17.79 (9.59)	21.43 (11.80)	1.93
Pain Unpleasantness	13.06 (10.66)	17.91 (12.55)	2.92
High-cued ratings (0 – 100)			
Anticipatory Anxiety	36.51 (20.33)	50.31 (19.00)	8.20**
Pain Intensity	63.02 (9.39)	66.75 (12.72)	1.88
Pain Unpleasantness	58.50 (15.30)	63.72 (14.51)	2.05

FFMQ (Five Facet Mindfulness Questionnaire), IUS-12 (Intolerance of Uncertainty – Short Form), PCS (Pain Catastrophizing Scale); scale ranges are provided alongside each measure.
Note: *** = p < .001, ** = p < .01, * = p < .05.

4.3.2 State mindfulness and catastrophizing measures

Between-group multivariate comparisons revealed that the HTM group scored significantly higher on the TMS ($F(1,66) = 11.79$, $p < .01$, $\eta_p^2 = .15$) and MAAS ($F(1,66) = 9.85$, $p < .01$, $\eta_p^2 = .13$) questionnaires, compared to the LTM group. The two groups did not differ on SCS scores, $F(1,66) = 1.39$, $p > .10$, $\eta_p^2 = .02$.

Table 2. Mean (SD) and F values for state measures.

	HTM (N = 36)	LTM (N = 32)	F(1, 66)
SCS (0 – 4)	0.74 (0.65)	0.93 (0.66)	1.39
TMS (0 – 4)	2.53 (0.51)	2.05 (0.64)	11.79**
Curiosity	2.68 (0.81)	2.15 (0.93)	6.34*
Decentering	2.41 (0.54)	1.97 (0.64)	9.47**
MAAS	4.89 (0.90)	4.03 (1.35)	9.85**

SCS (Situational Catastrophizing Scale), TMS (Toronto Mindfulness Scale), MAAS (Mindful Attention Awareness Scale).
Note: *** = $p < .001$, ** = $p < .01$, * = $p < .05$.

4.3.3 Group differences in cue-induced anxiety and pain modulation

Anticipatory Anxiety

A two (Group: high vs. low trait mindfulness) x three (Cue Type: low vs *novel* vs high) mixed ANOVA conducted on anticipatory anxiety ratings revealed a significant main effect of Group, with the HTM group reporting lower overall anticipatory anxiety ratings than the LTM group, $F(1,66) = 5.43$, $p = .02$, $\eta_p^2 = .08$. In addition, we also found a significant effect of Cue Type, $F(1.58,103.99) = 90.74$, $p < .001$, $\eta_p^2 = .58$. Sidak-corrected follow-up pairwise comparisons revealed that low-cued trials induced significantly lower anxiety levels relative to novel-cued trials ($t(67) = -11.45$, $p < .001$), while high-cued trials induced higher anxiety levels than novel-cued trials ($t(67) = 4.02$, $p < .001$). The Group x Cue Type interaction effect was not significant ($F(1.58,103.99) = 0.97$, $p > .10$, $\eta_p^2 = .01$).

Between group comparisons conducted on computed conditioned hypoalgesia (difference in ratings between novel-cued and low-cued trials) and conditioned hyperalgesia (i.e., difference between high-cued and novel-cued trials) difference scores for anticipatory anxiety ratings did not show any significant group differences (p's all > .10).

Pain Intensity

The two (Group: high vs low trait mindfulness) x three (Cue Type: low vs novel vs high) mixed ANOVA conducted on pain intensity ratings again revealed a main effect of Group, with the HTM reporting lower overall pain intensity ratings than the LTM group, $F(1,66) = 4.52$, $p = .04$, $\eta_p^2 = .06$. There was also a significant main effect of Cue Type, $F(1.29,85.27) = 261.66$, $p < .001$, $\eta_p^2 = .80$. Low-cued trials resulted in lower pain intensity ratings relative to novel-cued trials ($t(67) = -16.26$, $p < .001$), while high-cued trials resulted in higher pain intensity ratings than the novel-cued trials ($t(67) = 12.99$, $p < .001$) . The Group x Cue type interaction effect was not significant ($F(1.29,85.27) = 1.15$, $p > .10$, $\eta_p^2 = .02$).

Furthermore, analyses of the computed difference score also showed no significant group differences in computed conditioned hypoalgesia ($t(66) = 0.43$, $p > .10$) or conditioned hyperalgesia ($t(64.94) = 1.22$, $p > .10$) difference scores for pain intensity ratings.

Pain Unpleasantness

The two (Group: high vs. low trait mindfulness) x three (Cue Type: low vs. novel vs high) mixed ANOVA conducted on pain unpleasantness ratings revealed a main effect of Group, with the HTM group reporting lower overall pain unpleasantness ratings than the LTM group, $F(1,66) = 4.16$, $p < .05$, $\eta_p^2 = .06$. There was also a significant main effect of Cue Type, $F(1.29,84.90) = 203.39$, $p < .001$, $\eta_p^2 = .76$. Low-cued trials resulted in lower pain unpleasantness ratings relative to novel-cued trials ($t(67) = -12.86$, $p < .001$), while high-cued trials resulted in higher pain unpleasantness ratings than the novel-cued trials ($t(67) = 11.90$, $p < .001$). The analyses also revealed a significant Group x Cue Type interaction effect, $F(1.29,84.90) = 4.81$, $p = .02$, $\eta_p^2 = .07$. Sidak-adjusted follow-up pairwise comparisons showed lower pain unpleasantness ratings on the high-cued trials in the HTM group compared to the LTM group ($t(66) = 2.65$, $p < .01$). There were no group differences in pain unpleasantness ratings on low-cued and novel-cued trials (p's all > .10).

Between group comparisons conducted on the computed difference scores for pain unpleasantness ratings similarly revealed that the high mindfulness group showed reduced conditioned hyperalgesia ($t(66) = 2.33$, $p = .02$) relative to the low trait mindfulness group. There were no group differences in conditioned hypoalgesia ($t(66) = 1.21$, $p > .10$).

Anticipatory anxiety, pain intensity and pain unpleasantness ratings on low, novel and high-cued trials are illustrated in Figure 2. Computed difference scores for conditioned hypoalgesia and hyperalgesia across both groups are illustrated in Figure 3.

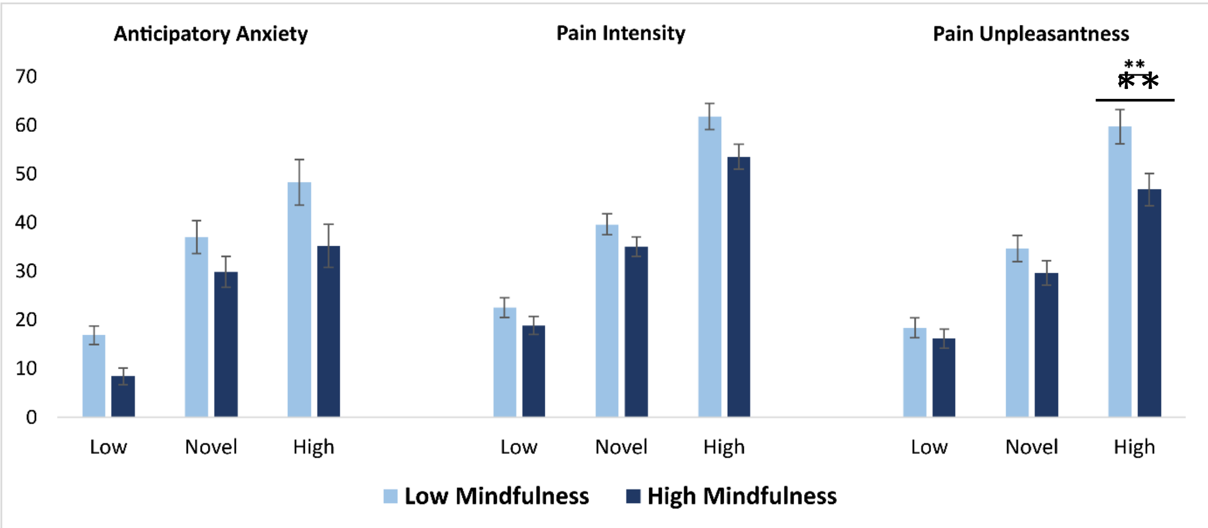

Figure 2. Mean anticipatory anxiety, pain intensity and pain unpleasantness ratings on low, novel and high-cued trials across both groups. Error bars indicate standard errors. ** = *p* < .01. Note that we only marked significant interactions between Group and Cue Type, but not significant main effects for visual clarity purposes.

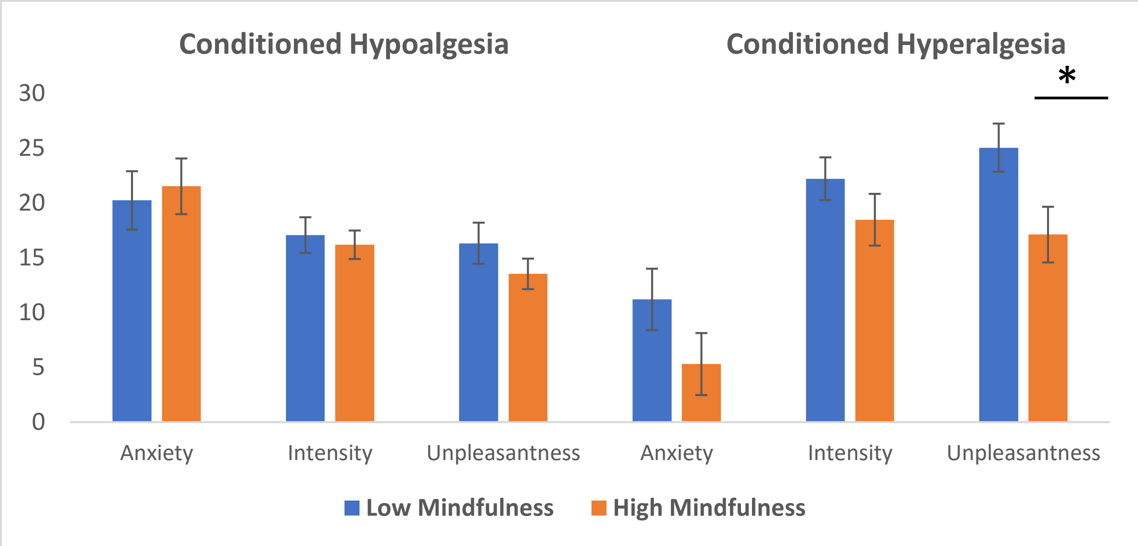

Figure 3. Computed conditioned hypoalgesia and hyperalgesia magnitudes (using a difference score approach) across both groups. Error bars indicate standard errors. * = *p* < .05. Note that we only marked significant interactions between Group and Cue Type, but not significant main effects for visual clarity purposes.

4.3.4 Cue-induced anxiety and pain modulation: Associations with trait and state mindfulness and pain catastrophizing measures

We first ran preliminary two-tailed Pearson correlations to probe potential links between the self-report mindfulness and pain catastrophizing questionnaires and the VAS ratings on the (unconditioned) novel-cued trials (see Table 3). The correlational analyses revealed that state catastrophizing was associated with significantly higher anticipatory anxiety, pain intensity and pain unpleasantness ratings on novel-cued trials. Higher intolerance of uncertainty and trait pain catastrophizing were linked to higher anticipatory anxiety levels, while MAAS scores were negatively associated with novel-cued anticipatory anxiety.

Table3. Correlations between the self-report questionnaires and VAS ratings on novel-cued (unconditioned) trials

	Novel-cued trials		
	Anxiety	Intensity	Unpleasantness
Group	-.19	-.19	-.17
IUS	.26*	.06	.12
PCS	.29*	.06	.12
SCS	.42***	.45**	.39**
MAAS	-.27*	-.24	-.13

TMS	-.19	-.05	-.06

We then conducted partial two-tailed correlational analyses to test for potential associations between the self-report questionnaires and anticipatory anxiety, pain intensity and pain unpleasantness ratings on the low and high pain-cued trials (after controlling for VAS ratings on novel-cued trials) (see Table 4). The analyses showed that higher levels of intolerance of uncertainty were associated with higher pain intensity and pain unpleasantness ratings on high-cued trials. We also found positive correlations between both trait and state catastrophizing scores and anticipatory anxiety ratings on high-cued trials. For low-cued trials, higher TMS scores were linked to reduced anticipatory anxiety levels.

Table 4. Partial correlations between the self-report questionnaires and VAS ratings on low and high pain-cued trials (controlling for ratings on novel-cued trials)

	Low-cued trials			High-cued trials		
	Anxiety	Intensity	Unpleasantness	Anxiety	Intensity	Unpleasantness
Group	-.33**	-.03	.05	-.16	-.19	-.28
IUS	.03	-.18	-.21	.23	.29*	.34**
PCS	.03	-.23	-.25	.34**	.28*	.20
SCS	.09	.01	.01	.29*	.18	.14
MAAS	.05	.04	.06	-.10	-.13	-.15
TMS	-.26*	.08	.21	.05	-.15	-.19

4.4 Discussion

In the present study, we aimed to investigate the influence of trait mindfulness level on the modulation of expectancy-induced perceptual biases during an explicit pain conditioning paradigm. The analyses revealed that the HTM group reported lower overall anticipatory anxiety, pain intensity and pain unpleasantness ratings relative to the LTM group during the testing phase. In line with our hypotheses, the HTM group also reported reduced cue-induced hyperalgesic effects when compared to the LTM group. However, this group difference was significant only for pain unpleasantness ratings, although a similar trend was observed for anticipatory anxiety and pain intensity ratings. Given the explicit nature of our conditioning procedure, it is unlikely that these group differences in cue-induced hyperalgesia were the results of differential learning processes across trait mindfulness level. Crucially, there were no group differences in (unconditioned) novel-cued trials suggesting that the reduced conditioned hyperalgesia in the HTM group was likely driven by a reduced sensitivity to the influence of the high pain cue on pain experience. However, contrary to our expectations, we failed to observe the hypothesised group differences in the modulation of cue-induced hypoalgesia.

This pattern of results is different to what we observed in our previous study (Vencatachellum et al., 2021). In that particular study, we found evidence of attenuated conditioned hypoalgesic effects, but not of conditioned hyperalgesic effects, following the instructed use of a mindfulness strategy (relative to a suppression strategy). The current study revealed the opposite pattern. In the following sections, we consider potential explanations for this disparity in findings between the two studies.

In our previous study, we opined that, due to its brevity, our mindfulness induction condition may have lacked the modulatory power to successfully mitigate the pervasive effects of negative expectations on pain perception. As highlighted previously, conditioned hyperalgesic effects can prove particularly resistant to extinction processes (Colagiuri et al., 2015; Colloca et al., 2008). Furthermore, neuroimaging studies employing similar brief mindfulness training approaches (Zeidan et al., 2011; Zeidan et al., 2015) have reported different patterns of neural activation to those observed in experienced meditators (Grant et al., 2011; Lutz et al., 2013) or individuals with high dispositional mindfulness levels (Harrison et al., 2019; Zeidan et al., 2018). These studies have observed increased activation of prefrontal cortices during pain stimulation in novice meditators, which the authors have typically interpreted as a reflection of the higher regulatory effort required to maintain non-evaluative attentional focus in early learning stages of mindfulness practice. The high affective valence of the high pain cue may thus have taken precedence over the non-elaborative prescriptions encouraged by the mindfulness instructions, although this is largely speculative at this point. Nonetheless, in our rationale for the current study, we argued that high trait mindfulness levels may better mimic the modulatory properties of extensive mindfulness practice. The present findings, along with those of Taylor et al.'s (2018) who observed similar reductions in conditioned hyperalgesic effects in a sample of expert meditative practitioners, seem to support this assertion.

This explanation, however, does not account for the absence of the hypothesized group differences in conditioned hypoalgesic effects in the current study. This could be attributed to another methodological difference between the two studies. Contrary to our previous study (Vencatachellum et al., 2021), participants in the present study were explicitly informed about the cue-stimulus contingencies prior to the acquisition phase. Although post-experimental manipulation checks in our first study did confirm that participants successfully detected the (implicit) cue-stimulus contingency, previous research has shown that explicit conditioning approaches tend to elicit markedly stronger conditioned effects compared to implicit conditioning approaches (Bartels et al., 2014; Martin-Pichora et al., 2011). Accordingly, we observed larger effect sizes of conditioned hypoalgesia (η_p^2 = .78 vs .37 for intensity, and η_p^2 = .70 vs .37 for unpleasantness ratings) and hyperalgesia (η_p^2 = .73 vs .45 for intensity and η_p^2 = .69 vs .38 for unpleasantness ratings) in the current, relative to our previous, study. A consequence of these enhanced conditioning effects, however, is that we noticed a floor effect for pain intensity and pain unpleasantness ratings on low-cued trials (i.e., intensity and unpleasantness ratings were skewed towards the minima of the VAS scales). Consequently, it is possible that this floor effect may have hindered our analytical potential for probing group differences in the magnitude of conditioned hypoalgesic effects.

Although our two studies bore different patterns of results, they do provide supporting evidence for the proposal that mindfulness may mitigate the biasing influence of expectations on pain experience. The present finding that trait mindfulness is linked to reduced sensitivity to conditioned hyperalgesic effects is of particular clinical relevance. Evidence from neurobiological studies suggest that several of the neural substrates associated with nocebo hyperalgesia may also be implicated in the amplification and chronification of pain (Thomaidou et al., 2021). Our correlational analyses also revealed that higher levels of pain catastrophizing and intolerance of uncertainty were linked to increased conditioned hyperalgesia. Importantly, both factors have previously been identified as potential risk factors in the development, magnification and maintenance of acute and chronic pain (e.g., Burns et al., 2015; Donthula et al., 2020; Kneeland et al., 2019; Neville et al., 2021; Severeijns et al., 2001). Promisingly, in addition to the attenuated conditioned hyperalgesic effects, trait mindfulness was also linked to lower levels of trait pain catastrophizing and intolerance of uncertainty. Although a dispositional quality, previous studies have shown that intensive mindfulness training can lead to significant increases in trait mindfulness levels over time (Kiken, 2015; Orzech, 2009). Our findings therefore suggest that cultivation of mindfulness may acts as a potential buffer against the amplificatory influence of pain catastrophizing and intolerance of uncertainty on conditioned hyperalgesia.

The current study adds to the growing empirical interest in the modulatory impact of mindfulness on expectancy-driven perceptual biases. This amassing, but still equivocal, evidence also serves to highlight important methodological considerations and their potential impact on such investigations. Despite these methodological issues, our study provides additional support for the notion that the cultivation of mindfulness can lessen the influence of prior expectations on pain experience and may thus provide a promising avenue for countering the hyperalgesic effects of pain catastrophizing and intolerance of uncertainty.

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5 General Discussion

The present project aimed to investigate the modulatory influence of mindfulness on pain expectancy-driven perceptual biases. More specifically, we tested the proposal that mindfulness may mitigate the biasing influence of prior expectations and information on pain perception and pain-related decision-making processes, across three separate pain expectancy-manipulation paradigms.

5.1 Summary of findings

5.1.1 Brief mindfulness training can mitigate the influence of priors on pain perception

Using an implicit classical pain cueing approach, we investigated whether the instructed use of a mindfulness strategy vs. an alternative cognitive regulatory strategy (i.e., suppression) differentially modulates conditioned hypoalgesic and hyperalgesic effects. The results revealed that while participants assigned to the suppression condition exhibited preserved cue-induced hypoalgesic effects, no such effects were observed for the mindfulness condition. Importantly, there were no group differences in pain ratings on unconditioned trials, suggesting that the absence of conditioned hypoalgesic effects in the mindfulness group was specifically driven by modulation of the influence of the low pain cue on pain experience, rather than a result of weaker pain alleviating effects.

However, we failed to observe the hypothesized mindfulness-induced reductions in conditioned hyperalgesia. We speculated that, due to its brevity, the mindfulness induction might have lacked the necessary modulatory power to mitigate conditioned hyperalgesic effects, given their increased resistance to extinction processes (Colagiuri et al., 2015; Colloca et al., 2008). The finding that the mindfulness group scored higher than the suppression group on the decentering subscale of the Toronto Mindfulness Scale (Lau et al., 2006), but not on overall state mindfulness, further supports this possibility.

5.1.2 Categorization alters perception: The pervasive biasing effects of category labels on pain perception and decision-making

We first aimed to replicate van der Meulen et al.'s (2017) findings that abstract categorical information can significantly alter pain perception and decision-making processes. Using a slightly modified version of the pain categorization paradigm, we found that that category labels resulted in increased perceived similarity (i.e., reduced variability in pain unpleasantness ratings) for stimuli within the same categories, relative to stimuli attributed to separate categories. Furthermore, participants assigned to the categorization condition reported lower confusion frequencies for stimuli at the category border compared to the control group. Overall, we successfully replicated the assimilation and accentuation effects reported by van der Meulen et al. (2017).

In a follow-up study, we tested whether these categorization-induced biases could be modulated by trait mindfulness level. Response patterns across both groups closely mirrored those observed within the categorization group in Study 2(a), suggesting that the paradigm was likely successful in eliciting the hypothesised categorization effects. However, contrary to our expectations, we failed to observe any differences between high trait mindfulness scorers and low trait mindfulness scorers in the modulation of assimilation and accentuation effects in both the learning phase and the recall phase.

5.1.3 Reduced vulnerability to conditioned hyperalgesia in highly mindful individuals

Our third study aimed to address the methodological considerations raised in our Study 1 (Vencatachellum et al., 2021). We investigated whether individuals high in trait mindfulness level (as assessed by the Five Facet Mindfulness Questionnaire; Baer et al., 2006) demonstrate reduced conditioned hypoalgesic and hyperalgesic effects relative to low trait mindfulness individuals. The study also employed an explicit conditioning paradigm to rule out the possibility that any resultant group differences in pain reports could be attributed to differential learning processes across trait mindfulness level. The analyses revealed that high trait mindfulness scorers reported smaller cue-induced hyperalgesic effects for pain unpleasantness ratings compared to low trait mindfulness scorers. There were, however, no group differences in cue-induced hypoalgesia, potentially attributable to a floor effect in pain ratings on low-cued trials.

5.1.4 Synthesis

Although they revealed slightly different modulatory patterns, the findings from our two pain conditioning studies altogether provided supporting evidence for the notion that mindfulness may mitigate sensitivity to pain conditioning procedures.

Importantly, these reductions in conditioned hypoalgesic and hyperalgesic effects could not be accounted for by an attenuation of learning processes in mindfulness. Post-experimental manipulation checks in Study 1 revealed that participants assigned to the mindfulness condition reported equivalent cue-stimulus contingency awareness to the suppression group. In Study 3, we aimed to further minimise the potential confounding influence of differential learning processes by explicitly informing participants of the cue-stimulus contingency prior to the acquisition phase. Our findings, therefore, suggest that mindfulness may dampen the influence of prior (cued) information on pain perception, whilst preserving awareness of the cue-stimulus contingency. This interpretation is further supported by evidence from Taylor et al. (2018), who reported similar reductions in conditioned hyperalgesia in a sample of experienced meditators. Crucially, they also demonstrated that extensive mindfulness practice does not weaken the critical ability to detect and learn from associative information (as evidenced by preserved cue-evoked anticipatory skin conductance responses). Instead, they opined that meditation experience may alleviate cue-induced hyperalgesia by mitigating the impact of such associative processes on the conscious percept. Overall, published evidence from pain conditioning studies has thus far provided initial support for the notion that the stance of heightened sustained non-elaborative monitoring of present-moment experience during mindfulness may lead to a reduction in the biasing influence of prior cognitive and emotional expectations on perception.

However, we failed to observe similar reductions in the expectancy-driven perceptual biases elicited by our pain categorization paradigm. We considered several potential explanations for the disparate findings between the conditioning and categorization paradigms, including potential disparity in resistance to modulation, the general subtlety of categorization effects and potential methodological differences (e.g., the unchanged label-stimulus contingency throughout both learning and recall phases). However, any definitive explanation is largely limited by the novelty of the paradigm. The neural mechanisms underlying pain categorization are yet to be investigated and therefore constitute a particularly intriguing avenue for future research.

5.2 Theoretical and methodological considerations

The findings from our pain conditioning studies, together with those from Taylor et al. (2018), constitute important first forays in the empirical validation of recently formulated predictive processing models of mindfulness positing that the perceptual process during a mindful state is less likely to be constrained by pre-existing expectations or beliefs. More precisely, according to this framework, sustained mindful attention toward the ongoing influx of physical and mental phenomena serves to drive an increase in the precision (signal-to-noise ratio) of ascending exteroceptive, proprioceptive, nociceptive and interoceptive sensory signals (Farb et al., 2015; Lutz et al., 2019; Manjaly & Iglesias, 2020; Pagnoni, 2019). At the same time, the re-orienting of attention away from automatically activated mental distractors and back to the non-judgmental monitoring of the present moment experience is believed to lead to a relaxation of the precision afforded to prior cognitive and affective expectations, beliefs or desires. Proponents of these models have typically called upon neuroimaging studies of mindfulness-driven pain modulation as supporting evidence for these claims. These studies have commonly revealed that mindfulness-induced pain relief is accompanied by a seemingly unique neural pattern involving increased activation of pain-related sensory processing regions and reduced activation of memory-based and cognitive-affective regions (Gard et al., 2012; Grant et al., 2011; Lutz et al., 2013). While the proposed prioritization of afferent sensory information and downweighing of prior beliefs and expectations provide an attractive explanatory framework to account for the aforementioned pattern of neural activity during mindful pain regulation, this interpretation is not exempt from potential logical fallacies attached to a pure ‘reverse inference’ approach, i.e., inferring specific cognitive processes based on observed brain activation without direct testing of said cognitive processes. In other words, there is the danger that the observed neural mechanisms of mindfulness are themselves being interpreted post-hoc with preconceived beliefs about mindfulness in mind. Our approach helped to address this issue by directly manipulating both prior information (in the form of pain cues or labels) and the incoming sensory information (in the form of varying thermal heat stimuli).

Importantly, we demonstrated in Study 1 that brief mindfulness instructions could significantly reduce the magnitude of conditioned hypoalgesic effects in addition to the previously reported reductions in conditioned hyperalgesia in experienced meditators (Taylor et al., 2018) (which we successfully replicated in Study 3 with high trait mindfulness individuals), as would be predicted by the aforementioned models. Interestingly, the observed mindfulness-induced reduction in conditioned hypoalgesia is also consistent with a series of recent studies contrasting the underlying mechanisms involved in mindfulness vs placebo-driven hypoalgesia. More precisely, these studies aimed to investigate the extent to which the hypoalgesic effects of mindfulness and placebo procedures are mediated by endogenous opioidergic systems (Adler et al., 2016; Case et al., 2022; May et al., 2018; Wells et al., 2020; Zeidan et al., 2016). To do so, participants were administered the opioid antagonist naloxone during either a mindfulness training, a placebo or a non-manipulation control condition. The results revealed that the naloxone infusion successfully negated the pain-relieving effects of the placebo procedure. In contrast, the opioid blockade failed to reverse the mindfulness-induced hypoalgesic effects. These findings further support the notion that mindfulness may alleviate pain via unique neurochemical pathways that do not rely on endogenous opioidergic mechanisms.

Altogether, evidence from studies investigating mindfulness-driven modulation of conditioned hypoalgesia/hyperalgesia and placebo hypoalgesia is so far largely consistent with the predictive processing view of mindfulness. While the current project, along with Taylor et al.'s study (2018), constitute the first empirical attempts at directly testing hypotheses derived from this predictive processing viewpoint, evidence from other research domains have also lent circumstantial support to this framework. These evidence range from mindfulness-induced reductions in classically conditioned responding (Hanley & Garland, 2019), habitual responding following implicit learning (Whitmarsh et al., 2013), craving and craving-related behaviours (Tapper, 2018), implicit age and race biases (Lueke & Gibson, 2014), automatic stereotype-activated behaviours (Djikic et al., 2008), vulnerability to the sunk-cost bias (Hafenbrack et al., 2013) and cognitive rigidity (Greenberg et al., 2012); findings that are all consistent with a reduced influence of priors on behaviour and perception. Similarly, recent neuroimaging studies have also shown that mindfulness practice can also attenuate reward prediction signals to appetitive stimuli (Kirk & Montague, 2015; Kirk et al., 2019).

However, it is important to note that even though our findings lend partial support to a predictive processing understanding of mindfulness-driven perceptual modulation, our studies did not aim to provide a direct investigation of the computational and neurophysiological mechanistic postulates inherent to these models. While our results are consistent with the proposed model, they cannot speak to the superiority of the predictive processing model over other Bayesian or reinforcement-learning models. Furthermore, the observed reductions in conditioned hypoalgesia and hyperalgesia could be explained by either a reduced influence of priors during the perceptual process, an increased influence of sensory afferents or a combination of both. Our chosen methodological designs however do not allow us to tease apart the relative contributing influence of ascending sensory prediction errors vs precision afforded to prior information to the observed perceptual outcomes. Nevertheless, recent developments in computational modelling of trial-by-trial changes across expectancy manipulation paradigms (e.g., Hoskin et al., 2019) and the use of effective connectivity assessment of corresponding neural pathways (e.g., Sevel et al., 2015) provide promising approaches for addressing these questions.

The asymmetrical patterns of results that we observed across our three studies also serve to further highlight a growing methodological concern regarding the impact of mindfulness operationalization on experimental outcomes (Davidson, 2010). Across the empirical literature, mindfulness has been operationalized using a wide variety of assessment, training and manipulation approaches. These include brief mindfulness induction, explicit verbal instructions, trait and state self-report measures, and comparisons between novice vs experienced meditators or across individuals pre- vs post-mindfulness intervention/training. Likewise, across the current project, we employed a combination of such approaches including trait and state self-reports, as well as brief audio and text instructions. These different operationalisation approaches are typically highly inter-correlated. For instance, significant positive correlations are commonly reported between the various existing trait and state self-report measures (e.g., Bravo et al., 2017; Kiken et al., 2015; Siegling & Petrides, 2014), while experienced meditators and individuals who have undergone mindfulness training do usually report higher self-reported mindfulness levels compared to controls (e.g., Josefsson et al., 2014; Soler et al., 2014). It is thus not unreasonable to posit that this shared commonality between these different approaches can be conceptualised as ‘mindfulness’. Observation of similar experimental outcomes across different operationalisation methods can therefore allow us to conclude with greater confidence that the observed effects are indeed down to the construct of mindfulness. The downside to this scattergun approach, however, is that it can be difficult to determine whether any disparities in observed outcomes are due to differences in experimental paradigms used or instead due to the differences inherent to the various types of mindfulness operationalisation used. In spite of their aforementioned inter-correlations, different mindfulness operationalisations have at times also been shown to result in different behavioural, psychophysiological and neural outcomes. For instance, in Study 1 we found that both the brief mindfulness induction and higher state mindfulness levels were associated with reduced conditioned hypoalgesic effects, but no such predictive influence of trait mindfulness level.

Furthermore, our participant samples across our three studies consisted exclusively of non-meditators. We opted to investigate the modulatory influence of brief mindfulness instructions and trait mindfulness level in non-meditators as that approach offered us greater control over potential confounding factors. For instance, group differences between experienced and novice/non-meditators may not only reflect differences in mindfulness level but are also liable to potential differences in pre-selection biases (e.g., commitment to self-improvement, diet, lifestyle, attitude towards alternative vs pharmacological medicine) and demand characteristics (e.g., motivation, social desirability, expectation of mindfulness-related relief). Nonetheless, although our focus on non-meditators helps in mitigating these pre-selection biases, investigation of mindfulness-related outcomes within samples of non-practitioners is not devoid of methodological drawbacks. As we highlighted in Study 1, our brief mindfulness induction condition is unlikely to instigate mindful states phenomenologically equivalent to those experienced by accomplished mindfulness practitioners. This was supported by the fact that the mindfulness induction group scored higher on the decentering subscale of the Toronto Mindfulness Scale but not on overall state mindfulness level. This is also further evidenced by the differential patterns of neural activation typically observed in neuroimaging investigations of the pain alleviating effects of brief mindfulness training compared to extensive mindfulness meditative practice (Jinich-Diamant et al., 2020). Recruitment of, and subsequent comparisons between, high and low trait mindfulness scorers in Study 2 and 3 helped to overcome this issue. The high trait mindfulness group reported higher state mindfulness levels than the low trait mindfulness group across both studies. Furthermore, neuroimaging studies of pain modulation in highly mindful non-meditators have previously been shown to closely replicate neural activation patterns typically observed among experienced mindfulness practitioners (Harrison et al., 2019).

However, this approach is not without its own limitations. As is commonly the case with self-report instruments, mindfulness self-reports are not immune to the pitfalls of introspection. A key unresolved question is the extent to which non-meditators can reliably report on the magnitude and/or quality of their mindfulness. First, it remains to be established whether non-meditators and experienced meditators differ in their comprehension and interpretation of self-report items pertaining to the mindfulness construct. Secondly, it is important to determine how accurately higher scores on these scales actually capture enhanced mindfulness levels as opposed to participants' metacognitive beliefs in their mindfulness level or participants' desire to be mindful. Thirdly, potential individual differences in introspective ability or sensitivity constitute another relevant methodological concern. Mindfulness training practices are often highly introspective in nature, with techniques encouraging awareness and sustained monitoring of inner experiences. Accordingly, previous studies have linked meditation experience, mindfulness training and high trait mindfulness to improved introspective insight, metacognitive ability and body awareness accuracy (Baird et al., 2014; Fox et al., 2012; Nyklíček et al., 2020; Treves et al., 2019). Conversely, one cannot rule out the possibility that non-meditators and low mindful individuals may not actually be aware of their lack of mindfulness. As such, there is a risk of running into a circularity issue when asking participants to report (i.e., introspect) on their mindfulness level, whereby differences in reported mindfulness scores may instead reflect differences in introspective ability or style, rather than actual mindfulness levels. Tied in to this issue is evidence suggesting that the factor structure of some commonly used mindfulness questionnaire may differ between meditators and non-meditators (Pang & Ruch, 2019). Finally, given the increasing popularity of constructs like mindfulness, equanimity, acceptance and their potential benefits in clinical and non-clinical settings alike, the possibility of demand characteristics cannot be fully ruled out in samples of non-practitioners either (Jensen et al., 2012).

As such, a key ongoing challenge for the field of mindfulness research is to build a deeper understanding of how these different mindfulness operationalization approaches relate to each other, and their specific influence on commonly reported mindfulness-induced outcomes. Interestingly, recent years have seen a growing effort in devising potential behavioural measures of mindfulness that do not rely on self-report (Hadash & Bernstein, 2019a). These include the Breath Counting Task (Levinson et al., 2014), measures of sustained mindful awareness (Hadash et al., 2021), the self-distancing task (Shepherd et al., 2016), experience sampling of mind wandering (Killingsworth & Gilbert, 2010) and implicit measures of self-referential and selfless processing (Hadash & Bernstein, 2019b). However, these measures tend to tap into specific components of mindfulness, and it is therefore questionable as to how well they can capture the construct of mindfulness as a whole. Another intriguing, albeit costly, approach is the use of machine learning classifiers to distinguish between experienced and novice meditators, or different levels of the mindful state, based on their neurophysiological dynamics (Ahani et al., 2014, Pandey et al., 2021). While the prospect of a singular consensual operational measure of mindfulness is unlikely to be satisfied in coming years, the combination of the aforementioned self-report questionnaires, meditation expertise measure, behavioural assessment and neuro-physiological markers constitute an advisable approach and one which may also help in identifying the merits and limits of these different measures.

Finally, our results also highlight the importance of assessing both pain intensity and pain unpleasantness reports. While the two measures are usually positively correlated, previously reported neural correlates of pain intensity and unpleasantness reports suggest that they reflect different facets of the pain experience, i.e., a sensory-discriminative vs. an affective-motivational component, respectively (Auvray et al., 2010; Price & Harkins, 1992). This distinction may be of even greater relevance when it comes to the subjective experience of pain during mindfulness. As highlighted at the beginning of the thesis, early Buddhist scriptures posit that the mindful state allows the individual to fully experience the sensory component (i.e., the first arrow) of pain without the common urge to attribute to an affective value (i.e., the second arrow of pain) to the sensation. Accordingly, the increased somatosensory and insular activity, and concomitant de-activation of putatively cognitive-affective brain areas, during mindfulness-driven pain processing have been interpreted as reflecting this potential uncoupling of the sensory and affective dimensions of pain. Our results provide additional support for this notion. Of particular note, in Study 3, we observed significantly reduced conditioned hyperalgesia in the high trait mindfulness group for pain unpleasantness ratings but not for pain intensity ratings. This finding adds to a series of similar observations within the mindfulness literature linking mindfulness level and meditative experience to reductions in pain unpleasantness ratings but not in pain intensity ratings (Kohl et al., 2012; Perlman et al., 2010). Finally, our pain categorisation procedure in Study II(a) successfully elicited the hypothesised assimilation and accentuation effects in pain unpleasantness, but not pain intensity, reports. Interestingly, this finding closely replicated that previously reported by van der Meulen et al. (2017), raising the intriguing possibility that categorisation processes may differentially influence the sensory and affective components of pain.

5.3 Clinical implications

As highlighted previously, our findings that mindfulness may mitigate the influence of conditioned expectations on pain perception are consistent with previous evidence that administration of opioid antagonists negated placebo-induced hypoalgesic effects but not mindfulness-induced hypoalgesia (Case et al., 2021; May et al, 2018; Wells et al., 2020; Zeidan et al., 2015, 2016). In addition to the placebo response, these opioidergic mechanisms have also been shown to mediate the successful cognitive implementation of common regulatory strategies such as distraction, suppression, reappraisal and hypnosis (King et al., 2013; Sprenger et al., 2012). Altogether, these findings suggest that mindfulness-based interventions may provide a promising alternative to common cognitive regulatory strategies which are typically reliant on opioidergically-mediated pathways, and for those patients who may not benefit from opioid therapy.

One of the most promising aspects of precision-based computational models of psychopathology from a clinical perspective is their potential as a predictive tool for the identification of symptoms and patient samples that are most likely to benefit from specific interventions. The premise that mindfulness may help in relaxing the precision afforded to prior beliefs hold particular promise for the alleviation of symptomology that is characterised by hard-wired beliefs and behaviours. Importantly, chronic pain patients commonly report higher levels of organic pain beliefs, fear of pain, pain catastrophizing and rigid coping behaviours (Morley & Eccleston, 2004; Sturgeon & Zautra, 2013; Sullivan & D'Eon, 1990; Walsh & Radcliffe, 2002). Promisingly, the predictive processing viewpoint of mindfulness would suggest that mindfulness-based may be most effective for those patients with such high maladaptive beliefs and expectations. This perspective is supported by recent evidence showing that although participants did not show any differences in experienced pain during a mindfulness compared to a distraction manipulation, reported pain was significantly moderated by pain catastrophizing level (Prins et al., 2014). Participants with high dispositional pain catastrophizing reported lower pain levels during the mindfulness manipulation, while participants with low pain catastrophizing benefited most from the distraction manipulation.

By the same token, the hypothesised weighing of sensory information over prior information may also provide a potential pathway into identifying those clinical symptoms and conditions that are less likely to benefit from a mindfulness-based approach. While the clinical benefits of mindfulness have been the predominant targets of empirical enquiry, the possibility of mindfulness-induced adverse effects has been left largely unexplored. Yet, sparse reports, coming mainly from case and observational studies, have also documented such side, and even harmful, effects arising from mindfulness-based practice (Shapiro, 1992; Shonin et al., 2014). A corollary of the predictive processing view of mindfulness would be that mindfulness-based interventions may not be particularly well-suited to psychiatric symptoms and disorders which are characterised by sensory overload (i.e., sensory afferents that are unconstrained or poorly constrained by priors). Accordingly, the limited literature exploring potential adverse effects of mindfulness cautions against administration of mindfulness-related approaches to individuals with a history of psychotic or manic episodes (Chan-Ob & Boonyanaruthee, 1999; Disayavanish & Disayavanish, 1984; Kuijpers et al., 2007; Sethi & Bhargava, 2003; Walsh & Roche, 1979; Yorston, 2001). Interestingly, hallucinatory episodes during psychosis have been linked to a failure in attenuation of afferent sensory prediction errors (Adams et al., 2013; Brown et al, 2013; Heinks-Maldonado et al., 2007; Horga et al., 2014; Shergill et al., 2005, Sterzer et al., 2018). The predictive processing framework may thus provide a promising neurocomputational platform for exploring mindfulness-induced adverse effects, the mechanisms that may give rise to them and patient populations who may be most at risk of experiencing such effects.

Finally, we opted to focus specifically on mindfulness-driven pain modulation as the effects of prior expectations on pain perception have been particularly well documented across a series of existing pain expectancy manipulation paradigms. However, in contrast to other forms of clinical interventions, mindfulness practice is not typically aimed at addressing specific symptoms. Instead, improvements in symptomology are understood as resultant by-products of the everyday stance of non-judgemental, accepting form of awareness encouraged by mindfulness practice. As such, it is reasonable to expect that the proposed mitigation of habitual hard-coded beliefs and behaviours via mindfulness practice, and its aforementioned clinical implications, should be equally relevant to other sensory and affective domains.

5.4 Conclusion

This thesis set out to investigate an intriguing key prediction born out of recent predictive processing models of mindfulness, namely that the sustained non-judgmental attention to ongoing sensory experience may promote increased resistance to the well-documented biasing influence of prior expectations on perception. Our findings provided partial support for this notion, with brief mindfulness instructions and higher trait mindfulness levels linked to reduced conditioned hypoalgesic and hyperalgesic effects respectively. Although the primary aim of the current project was to further our mechanistic understanding of the processes underlying mindfulness-driven pain modulation, these results also bear clinically relevant implications. In particular, our findings also add to growing evidence suggesting that mindfulness may alleviate pain via neuropsychological mechanisms opposite to those typically observed in conditioning/placebo procedures, highlighting the potential of mindfulness-based interventions as a potential alternative to opioidergically-mediated regulatory strategies and medication. The presented evidence is also novel in that it suggests that mindfulness and expectancy-driven hypoalgesia may not only involve contrasting, but also counteracting, mechanisms. The investigation of the underlying mechanisms of mindfulness is still in its adolescence, and as with any nascent field of research, there are still many unknowns to be addressed (some of which were outlined at the concluding end of this thesis). Nevertheless, we believe that the methodological approaches employed within this research project, in conjunction with recently developed trial-by-trial computational modeling techniques and effective connectivity investigation of concomitant neural dynamics, constitute a highly promising avenue for deepening our understanding of the key mechanisms by which mindfulness conveys its beneficial (and potentially adverse) effects.

5.5 References

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Appendix

AppendixS1: Mindfulness and Suppression audio and text instructions

Mindfulness audio instructions (English version)

“As we begin this practice, allow your body to settle into a comfortable yet alert seated position
And, take a few moments to simply notice the sensations associated with your chosen posture
(15s break)

And, when you are ready, gently allow your attention to rest on your breathing
Not seeking to manipulate the breath in anyway
But, simply experiencing it as the air flows in and out of the body
(30s break)

You may find it useful to focus your attention on the part of the body where the breathing sensations are the most salient, the most obvious
Such as the expansion and contraction of the abdomen
Or the rise and fall of the chest
Or the inhaling and exhaling sensations located at the nostrils
(5s break)

Kindly bringing your attention to that particular location
And, following the rhythmic movements of the breath
Simply noticing the raw characteristics of these sensations
(1min break)

From time to time, you may notice that your mind begins to wander off,
Maybe to thoughts, images, sounds, memories, worries, fantasies,
Or maybe commentaries about how you are currently doing in the practice
That’s okay, that’s what minds do, they wander
And, whenever you notice that the mind has drifted off
Gently bring your attention back to the sensations of breathing
Back to the moment-to-moment observation of the flow of breathing
The breath can hence serve as an anchor to stabilise your attention on the present-moment experience.
One you can come back to at any moment
(1min break)

And, when you are ready, experiment with expanding your field of awareness to also include sensations, feelings and associated thoughts as they move through your mind
Again, the aim is not to try to induce these sensations, emotions or thoughts
Or to make sense of them
But simply noticing them as they enter your mind
Try to observe thoughts as mere events that come and go within the field of your consciousness
Without seeking to develop, judge or getting caught into them
Just observing and accepting them as they are
(1min break)

If you notice that your mind has been drawn into entertaining a particular pattern of thoughts,
Simply congratulate yourself on noticing that your mind has wandered off
And gently shift back into an observer stance
Using sensations of the breath and body, if need be, to stabilise your attention on the present moment experience
And, simply observing and allowing your experience to be as it is
(1min break)

You may find it useful to think of your mind as a wide blue sky,
And the arising thoughts and feelings as clouds
That come out of nowhere, change shape and fade away all on their own
There is no need to hold on to those thoughts or to push them away
Simply observing them as they appear, linger and drift away at their own rate
(5s break)

Hence, slowly developing a state of meta-awareness
As an observer of your own mind
And, an attitude of total openness towards all things that go through your mind"
(2 min)

Mindfulness text instructions (English version)

You will now receive a series of painful heat stimuli. Throughout this stimulation phase, we would like you to apply the instructions as described within the recording.
Your task is to cultivate a state of total openness and acceptance towards any sensory and emotional responses elicited by the heat stimuli. Try to simply observe any sensations, thoughts or feelings that arise during the stimulation, without judging or manipulating them. If you notice that your mind is drawn into entertaining this stream of thinking, kindly bring your attention back to the non-judgmental observation of these thoughts and feelings. Simply become aware of your current experience and allow it to be as it is. You may find it useful to think of your mind as a movie theater, whereby sensations, thoughts and feelings arising from the painful stimuli are like images being projected on a screen. And, you sit there in the audience simply observing these images as they come and go, without seeking to judge or develop them.

Suppression audio instructions (English version)

"As we begin this practice, take a moment and try to notice if there are any bodily sensations that are currently bothering you
You may notice sensations of discomfort, tension, fatigue, tightness, itch, pain or any other unwanted sensation
(5s break)

And, as soon as you notice any such sensation, try your best to mentally block it out
Your task is to try your best not to think about these sensations
The aim is not to observe or accept these sensations
Or even distract your mind away from them
But, instead, to prevent them from entering your conscious awareness
(5s break)

Whenever an unwanted sensation enters your mind, aim to remove it as quickly as possible
Concentrate on getting rid of any undesired sensation
(1min break)

Imagine that there are a few onlookers observing you during the practice
Your aim should be to continue to block unwanted sensations out of your mind
In such a way that these observers cannot tell what you are experiencing
You should try your best to suppress these sensations
Aim to fully block any external manifestations of your current state
(1min break)

As you focus on removing arising sensations, you may find that emotions associated with these sensations also become prominent
Again, as soon as you notice that any unwanted emotions or feelings enter your mind,
Try as hard as you can to put them away from your conscious awareness
These may be feelings of unpleasantness, restlessness, irritation, pain, etc...
Or they may even be unwanted emotions like sadness, anxiety or anger
That may be associated with anything that is bothering or upsetting you in your life generally
Your aim is again to try not to think about these unwanted feelings and emotions as they arise

Focus on suppressing these emotions in such a way that a person watching you would not know what you are feeling
(1min break)

Furthermore, I would like you to suppress any unwanted thoughts that crop up in your mind
These thoughts may be related to the current practice or the current session
Or they may be thoughts that come from elsewhere
Try your best to mentally block out these unwanted thoughts
Using all your mental power to force them out
Concentrate on getting rid of any unwanted thoughts that come to mind
And, again, behave in such a way that an observer could not guess what you are thinking of at the moment
(1min break)

Keep trying to suppress anything that is bothering you, stressing you, or upsetting you at the moment
Whenever unwanted thoughts, sensations or emotions enter your mind, focus on removing them as quickly as possible
Concentrate on mentally blocking them out of your conscious awareness
(30s break)

Watch out for upsetting thoughts, sensations and emotions, removing them each time they appear
Keep on practicing these instructions
All while making sure that you are concealing any external manifestations of what you are currently experiencing"
(2min break)

Suppression text instructions (English version)

You will now receive a series of painful heat stimuli. Throughout this stimulation phase, we would like you to apply the instructions as described within the recording.
Your task is to fully suppress any sensory and emotional responses elicited by the heat stimuli. Try as hard as you can, not to think about the sensations, thoughts and feelings that arise during the stimulation. If you still notice these, aim to mentally block them out as fast as you can. Concentrate on getting rid of any unwanted thoughts that come to mind.
You may find it useful to focus on not letting your feelings show while you receive the painful stimuli. In other words, you should aim to conceal any external manifestations of your experience; in such a way that a person watching you could not tell what you are feeling.

Mindfulness audio instructions (French version)
"Pour commencer cette pratique, permettez à votre corps de trouver une position assise à la fois confortable et éveillé
Et, prenez quelques instants à simplement observer les sensations liées à la posture choisie
(15s break)

Et, quand vous être prêt, laissez votre attention se poser tout doucement sur votre respiration
Sans chercher à manipuler le souffle de quelque façon
Simplement prendre conscience de l'expérience du souffle entrant et sortant du corps
(30s)

Vous trouverez peut-être utile de focaliser votre attention sur la partie du corps où les sensations respiratoires sont les plus saillantes, les plus flagrantes
Telle que l'expansion et la contraction de l'abdomen
Ou le gonflement et dégonflement de la poitrine
Ou les sensations inspiratoires et expiratoires au niveau des narines
(5s)

Portez tout doucement votre attention sur cet emplacement précis
Et, suivez les mouvements rythmiques du souffle
Observez tout simplement le caractère brut de ces sensations

(1min)

De temps à autre, vous remarquerez peut-être que votre esprit se met à se disperser,
Vers des pensées, des images, des sons, des souvenirs, des inquiétudes, des fantasmes
Ou se met peut-être à commenter votre performance quant à la pratique en cours
C’est tout à fait normal, c’est comme cela que fonctionne notre esprit, il vagabonde
Et, à chaque fois que vous constatez que votre esprit a été attiré ailleurs,
Ramener tout doucement votre attention vers les sensations respiratoires
Revenant vers une observation de chaque instant du cycle respiratoire
La respiration peut ainsi servir de point d’ancrage, permettant à notre attention de se stabiliser sur le moment présent.
Un point d’ancrage vers lequel vous pouvez retourner à tout moment
(1min)

Et, quand vous êtes prêt, essayez d'élargir le champ de votre attention afin d’y inclure les sensations, pensées et émotions qui traversent votre esprit
Une fois de plus, le but n’est pas d’essayer de provoquer ces sensations, pensées ou autres émotions
Ou de leur donner une signification
Mais simplement de les observer lorsqu'elles intègrent votre esprit
Essayez d’observer ces pensées comme de simples événements qui vont et viennent dans le champ de votre conscience
Sans chercher à les développer, à les juger ou à se laisser entraîner par ces pensées
Simplement les observer et les accepter telles quelles
(1min)

Si vous constatez que votre esprit s’est laissé prendre dans le fil de ces pensées
Vous pouvez vous féliciter d’avoir remarqué que votre esprit a été attiré ailleurs
Et revenez tout doucement vers cette perspective de simple observateur
Utilisant les sensations du souffle et du corps, s’il le faut, pour stabiliser votre attention sur l'expérience présente
Et, simplement observer et permettre à votre expérience d'être ce qu’elle est
(1min)

Vous trouverez peut-être utile d’imaginer que votre esprit est comme un ciel bleu et clair,
Et que les pensées et les émotions qui surviennent sont comme des nuages
Qui sortent de nulle part, changent de forme et disparaissent d’eux-mêmes
Il n’est nullement nécessaire de s’accrocher à ces pensées ou de les repousser
Simplement les observer qui apparaissent, subsistent et disparaissent à leur propre rythme
(5s)

Développant ainsi tout doucement une forme de méta-conscience
Où vous êtes observateur de votre esprit
Et, une attitude d’ouverture totale envers tout ce qui traverse votre esprit"
(2min)

Mindfulness text instructions (French version)

Vous allez maintenant recevoir une série de stimulations thermiques douloureuses. Au cours de cette séance de stimulation, nous voudrions que vous mettiez en pratique les instructions telles que décrites durant l'enregistrement audio.
Votre tâche est de contrôler et de résister à toutes réactions sensorielles et émotionnelles suscitées par la stimulation thermique. Essayez du mieux que vous pouvez de ne pas penser aux sensations, pensées et sentiments qui surviennent au cours de la stimulation. Si vous constatez que vous continuez à les remarquer, essayez de les bloquer hors de votre esprit aussi rapidement que vous le pouvez. Concentrez-vous sur le retrait de toutes pensées non-désirées de votre esprit.
Vous trouverez peut-être utile de vous efforcer à ne pas laisser entrevoir vos sentiments durant la réception des stimulations douloureuses. En d’autres mots, visez à dissimuler toute manifestation externe de votre expérience, de façon à ce qu’un individu vous observant ne puisse déterminer ce que vous ressentez.

Suppression audio instructions (French version)

“Pour commencer cette pratique, prenez un instant et essayez de remarquer s’il existe quelque sensation corporelle qui vous gêne en ce moment.
Vous remarquerez peut-être des sensations d’inconfort, de tension, de fatigue, de crispation, de démangeaison, de douleur ou autre sensation non-désirée
(5s break)

Et, aussitôt que vous prenez conscience de telles sensations, essayez de votre mieux de les maintenir hors de votre esprit
Votre tâche est d’essayer du mieux que vous pouvez de ne pas penser à ces sensations
Le but n'étant pas d’observer ou d’accepter ces pensées
Ou même de détourner votre esprit de ces pensées
Mais, plutôt, de les empêcher d'intégrer votre conscience
(5s)

A chaque fois qu’une sensation non-désirée intégré votre esprit, visez à l'éliminer au plus vite
Focalisez-vous sur l'élimination de toute sensation non-désirée
(1min)

Imaginez que vous soyez observé pendant la pratique
Votre but est de continuer à maintenir ces sensations non-voulues hors de votre esprit
De façon à ce qu’un observateur ne puisse déterminer ce que vous ressentez
Faites de votre mieux pour supprimer ces sensations
Visez à bloquer toute manifestation extérieure de votre expérience
(1min)

Pendant que vous vous appliquez à retirer les sensations qui apparaissent, vous noterez peut-être que des émotions liées à ces sensations peuvent aussi faire surface
A nouveau, aussitôt que vous remarquez que des émotions ou des sentiments indésirables intègrent votre esprit
Essayez du mieux que vous pouvez de les pousser hors de votre conscience
Elles peuvent prendre la forme de sentiments de désagrément, d’agitation, d’agacement, de douleur etc…
Ou même des émotions telles que la tristesse, l'anxiété ou la colère
Qui sont peut-être liées à toute chose qui vous dérange ou vous contrarie dans votre vie quotidienne
Votre but est, une fois de plus, de ne pas penser à ces sentiments et émotions non-désirées lorsqu’elles surviennent
Appliquez-vous à supprimer vos émotions de façon à ce qu’un individu vous observant ne puisse savoir ce que vous ressentez
(1min)

Et maintenant, je voudrais que vous essayiez de supprimer toute pensée non-voulue qui apparaisse dans votre esprit
Ces pensées peuvent être liées à la pratique ou à l'expérience en cours
Ou elles peuvent être des pensées venant d’ailleurs
Essayez de votre mieux de bloquer ces pensées indésirables hors de votre esprit
Utilisant toute votre capacité mentale pour les repousser
Concentrez-vous sur l'élimination de toute pensée non-désirée qui vous viennent à l’esprit
Et, une fois de plus, agissez de manière à ce qu’un observateur ne puisse deviner ce que vous avez à l’esprit en ce moment
(1min)

Continuez à essayer de supprimer tout ce qui vous dérange, vous stresse ou vous bouleverse en ce moment
A chaque fois que des pensées non-désirées intègrent votre esprit, appliquez-vous à les éliminer au plus vite
Concentrez-vous à les repousser hors de votre conscience
(30s)

Guettez toutes pensées contrariantes, les éliminant à chaque fois qu’elles apparaissent
Continuez à pratiquer ces instructions

Tout en veillant à dissimuler toute manifestation extérieure de ce que vous ressentez actuellement"
(2min)

Suppression text instructions (French version)

Vous allez maintenant recevoir une série de stimulations thermiques douloureuses. Au cours de cette séance de stimulation, nous voudrions que vous mettiez en pratique les instructions telles que décrites durant l'enregistrement audio.
Votre tâche est de cultiver une perspective d'ouverture et d'acceptation totale envers toutes réactions sensorielles et émotionnelles suscitées par la stimulation thermique. Essayez de simplement observer tous sensations, pensées et sentiments survenant au cours de la stimulation, sans chercher à les juger ou à les manipuler. Si vous constatez que votre esprit se laisse emporter à développer ce torrent de pensées, ramenez tout doucement votre attention vers l'observation sans jugement de ces pensées et de ces sentiments. Cherchez tout simplement à prendre conscience de votre expérience et de la permettre d'être ce qu'elle est.
Vous trouverez peut-être utile d'imaginer que votre esprit est comme une salle de cinéma, et que les sensations, pensées et sentiments suscités par les stimulations douloureuses sont comme des images qui sont projetées sur un écran. Et, vous êtes assis(e) là dans l'auditoire à simplement observer le va-et-vient de ces images, sans chercher à les juger ou à les développer.

Mindfulness audio instructions (German version)

"Zu Beginn dieser Übung setzen Sie sich bitte in eine bequeme aber ,wachsame Sitzposition.
Nehmen Sie sich ein paar Momente Zeit, um die Gefühle wahrzunehmen, die mit Ihrer gewählten Körperhaltung verbunden sind
(15s break)

Wenn Sie bereit sind, lassen Sie Ihre Aufmerksamkeit sanft auf Ihrer Atmung ruhen
Versuchen Sie, die Atmung nicht auf irgendeine Weise zu beeinflussen
Erfahren Sie einfach, wie die Luft in Ihren Körper hinein und wieder herausströmt
(30s)

Vielleicht hilft es Ihnen, Ihre Aufmerksamkeit auf den Teil Ihres Körpers zu richten, in dem Sie die Atmung am besten fühlen
z. B. beim Heben und Senken des Bauchs
Oder das Auf und Ab der Brust
Oder die Empfindung des Ein- und Ausatmens an den Nasenlöchern
(5s)

Lenken Sie Ihre Aufmerksamkeit auf diesen Punkt
Und folgen Sie den rhythmischen Bewegungen des Atems
Nehmen Sie einfach nur die diese Empfindungen wahr
(1min)

Von Zeit zu Zeit werden Sie bemerken, dass Ihr Geist anfängt zu wandern,
Vielleicht zu Gedanken, Bildern, Geräuschen, Erinnerungen, Sorgen, Fantasien,
Oder vielleicht zu Kommentaren darüber, wie gut Sie die Übung umsetzen
Das ist in Ordnung, das ist es, was Gedanken tun, sie wandern
Immer dann, wenn Sie merken, dass Ihre Gedanken wandern,
lenken Sie Ihre Aufmerksamkeit sanft zurück auf die Empfindung des Atmens
Zurück zur Beobachtung des Atemflusses von Augenblick zu Augenblick
Der Atem kann also als Anker dienen, um Ihre Aufmerksamkeit auf das momentane Erleben zu stabilisieren
Ein Anker, zu dem Sie jederzeit zurückkehren können
(1min)

Wenn Sie bereit sind, experimentieren Sie mit der Erweiterung Ihres Bewusstseinsfeldes, um auch Empfindungen, Gefühle und damit verbundene Gedanken mit einzubeziehen, während sie sich durch Ihren Geist bewegen
Auch hier geht es nicht darum, diese Empfindungen, Emotionen oder Gedanken zu induzieren
Oder um einen Sinn in Ihnen zu finden
Es geht vielmehr darum, sie einfach zu beobachten, wenn sie in Ihren Geist gelangen
Versuchen Sie, Gedanken als bloße Ereignisse zu betrachten, die sich in das Feld Ihres Bewusstseins bewegen und wieder daraus verschwinden

Ohne sie weiterzuentwickeln, sie zu beurteilen oder sich in sie hineinzusteigern
Sie einfach zu beobachten und sie so zu akzeptieren, wie sie sind
(1min)

Wenn Sie bemerken, dass Ihr Geist sich immer wieder mit einem bestimmten Gedanken beschäftigt,
Gratulieren Sie sich selbst einfach dazu, dass Sie bemerkt haben, dass Ihr Geist gewandert ist
Begeben Sie sich anschließend wieder sanft zurück in eine beobachtende Haltung
Verwenden Sie, wenn nötig, Atem- und Körperempfindungen, um Ihre Aufmerksamkeit auf den gegenwärtige Moment zu stabilisieren
Einfach nur zu beobachten und Ihre Erfahrung so sein zu lassen, wie sie ist
(1min)

Es könnte Ihnen helfen, sich Ihren Geist als einen weiten blauen Himmel vorzustellen,
Und die aufkommenden Gedanken und Gefühle als Wolken
Die aus dem Nichts kommen, ihre Form ändern und von selbst verblassen
Es gibt keinen Grund, an diesen Gedanken festzuhalten oder sie wegzudrängen
Beobachten Sie einfach, wie sie erscheinen, verweilen und in ihrer eigenen Geschwindigkeit davontreiben
(5s)

Langsam entwickelt sich dadurch ein Zustand des Meta-Bewusstseins
Und Sie werden zu einem Beobachter Ihres eigenen Geistes
Sie erlangen eine Haltung der völligen Offenheit gegenüber allen Dingen, die Ihnen durch den Kopf gehen"
(2min)

Mindfulness text instructions (German version)

Sie werden jetzt noch einmal eine Reihe von scherzvollen Hitzestimuli erhalten. Während dieser Stimulationsphase würden wir Sie gerne bitten, die Anleitungen die Sie in der Aufnahme gehört haben umzusetzen.
Ihre Aufgabe ist es, einen Zustand von kompletter Offenheit und Akzeptanz gegenüber allen sensorischen und emotionalen Empfindungen zu erreichen und erhalten, die durch den Hitzestimulus hervorgerufen werden. Versuchen Sie einfach nur jede Empfindung, jedes Gefühl und jeden Gedanken die während der Stimulation aufkommen, zu beobachten, ohne diese zu bewerten oder zu verändern. Wenn Sie merken, dass Ihr Geist von diesem Gedankenfluss abweicht, dann bringen Sie Ihre Aufmerksamkeit wieder vorsichtig zurück zur nicht-bewertenden Beobachtung dieser Gefühle und Gedanken. Werden Sie sich einfach der Situation wie Sie ist bewusst und erlauben Sie ihr so zu sein, wie sie ist.
Vielleicht hilft es Ihnen, Ihren Geist als eine Art Kino zu sehen, in welchem jede Empfindung, jedes Gefühl und jeder Gedanke die während der Stimulation aufkommen wie der Film sind, und Sie im Publikum sitzen und sich diese Bilder anschauen wie sie kommen und gehen, ohne dabei zu versuchen diese zu bewerten oder auszubauen.

Suppression audio instructions (German version)

Nehmen Sie sich zu Beginn dieser Übung einen Moment Zeit und versuchen Sie zu bemerken, ob es irgendwelche körperlichen Empfindungen gibt, die Sie momentan stören
Es könnte sein, dass Sie Unbehagen, Verspannungen, Müdigkeit, Anspannung, Juckreiz, Schmerzen oder andere ungewollte Empfindungen verspüren
(5s break)

Sobald Sie ein solches Gefühl bemerken, versuchen Sie nach Kräften, es mental zu blockieren
Ihre Aufgabe ist es, sich nach Kräften zu bemühen, nicht über diese Empfindungen nachzudenken
Es geht nicht darum, diese Empfindungen zu beobachten oder zu akzeptieren
Oder gar Ihren Geist von ihnen abzulenken
Es geht vielmehr darum, diese Empfindungen daran zu hindern, in Ihr Bewusstsein einzudringen
(5s)

Wann immer es ein ungewolltes Gefühl in Ihren Geist schafft, versuchen Sie, es so schnell wie möglich zu entfernen
Konzentrieren Sie sich darauf, jedes unerwünschte Gefühl loszuwerden
(1min)

Stellen Sie sich vor, es gibt ein paar Zuschauer, die Sie während des Trainings beobachten
Ihr Ziel sollte es sein, weiterhin unerwünschte Empfindungen aus Ihrem Geist zu verdrängen
Sodass diese Beobachter nicht sehen können, was Sie erleben
Sie sollten sich nach Kräften bemühen, diese Empfindungen zu unterdrücken
Versuchen Sie, alle äußeren Anzeichen Ihres aktuellen Befindens vollständig zu blockieren
(1min)

Da Sie sich darauf konzentrieren, aufkommende Empfindungen zu unterdrücken, könnten Sie feststellen, dass Emotionen, die mit diesen Empfindungen assoziiert werden, deutlicher werden
Sobald Sie also bemerken, dass unerwünschten Gefühle oder Emotionen in Ihren Geist eindringen,
Versuchen Sie nach Kräften, diese aus Ihrem Bewusstsein fernzuhalten
Dies können Gefühle wie Unwohlsein, Unruhe, Irritation, Schmerzen usw. sein ...
Dies können auch unerwünschte Emotionen wie Trauer, Angst oder Wut sein
Dies kann mit Dingen verbunden sein, die Sie in Ihrem Leben im Allgemeinen stören oder verwirren
Ihr Ziel ist es, zu versuchen, nicht über diese ungewollten Gefühle und Emotionen nachzudenken, während sie entstehen
Konzentrieren Sie sich darauf, diese Emotionen so zu unterdrücken, dass eine Person, die Ihnen zuschaut, nicht weiß, was Sie fühlen
(1min)

Außerdem möchte ich, dass Sie unerwünschte Gedanken, die in Ihrem Geist auftauchen, unterdrücken
Diese Gedanken können mit der gegenwärtigen Übung oder der aktuellen Sitzung zusammenhängen
Oder es können Gedanken sein, die von anders wo herkommen
Versuchen Sie nach Kräften, diese ungewollten Gedanken geistig zu verdrängen
Versuchen Sie mit all Ihrer mentalen Kraft, diese Gedanken loszuwerden
Konzentrieren Sie sich darauf, diese unerwünschten Gedanken loszuwerden, die es in Ihren Geist geschaff haben
Verhalten Sie sich so, dass ein Beobachter nicht erraten könnte, woran Sie gerade denken
(1min)

Versuchen Sie weiterhin, alles zu unterdrücken, was Sie beschäftigt, stresst oder im Moment verärgert
Wann immer unerwünschte Gedanken, Empfindungen oder Emotionen in Ihren Geist gelangen, konzentrieren Sie sich darauf, sie so schnell wie möglich zu entfernen
Konzentrieren Sie sich darauf, sie mental aus Ihrem Bewusstsein zu verdrängen
(30s)

Achten Sie auf störende Gedanken, Empfindungen und Emotionen und entfernen Sie diese jedes Mal, wenn sie auftauchen
Führen Sie diese Übung weiter aus
Und vergewissern Sie sich, dass Sie nicht nach außen zeigen, was Sie gerade erleben"
(2min)

Suppression text instructions (German version)

Sie werden jetzt noch einmal eine Reihe von scherzvollen Hitzestimuli erhalten. Während dieser Stimulationsphase würden wir Sie gerne bitten, die Anleitungen die Sie in der Aufnahme gehört haben umzusetzen.
Ihre Aufgabe ist es, alle sensorischen und emotionalen die durch den Hitzestimulus hervorgerufen werden gänzlich zu unterdrücken. Versuchen Sie so gut wie Sie können nicht an die Empfindungen, Gefühle und Gedanken zu denken, die während der Stimulation aufkommen. Wenn Sie Ihnen immer noch auffallen,

versuchen Sie diese so schnell wie möglich geistig zu blockieren und auszuklammern. Konzentrieren Sie sich darauf alle ungewollten Gedanken die Ihnen in den Kopf kommen loszuwerden.
Vielleicht hilft es Ihnen sich darauf zu konzentrieren, Ihre Gefühle nicht nach außen sichtbar zu machen während Sie die schmerzvollen Stimuli erhalten. Mit anderen Worten, Sie sollten versuchen alle äußeren Manifestationen Ihrer Erfahrungen zu verbergen; auf eine Art und Wiese, dass eine Person die Sie beobachtet nicht erkennen kann was Sie gerade fühlen.

AppendixS2: Toronto Mindfulness Scale
French version

Instructions: Nous sommes intéressés par votre expérience durant l'épreuve de stimulation thermique. Vous trouverez ci-dessous une liste d'énoncés décrivant ce qui peut être ressenti pendant l'épreuve. Veuillez lire chaque phrase. Chaque phrase est accompagnée de cinq choix possibles: "pas du tout", "légèrement", "moyennement", "largement", et "complètement". Veuillez indiquer à quel point vous approuvez de chaque proposition. En d'autres mots, à quel point l'énoncé correspond-elle à votre expérience ?	**Pas du tout**	**Légèrement**	**Moyennement**	**Largement**	**Complètement**
1. Je me suis senti(e) comme séparé(é) de mes pensées et de mes sentiments, ainsi que de leur caractère changeant.	0	1	2	3	4
2. J'étais plus préoccupé(e) à rester ouvert(e) à toute expérience, qu'à chercher à la contrôler ou à la modifier.	0	1	2	3	4
3. J'étais curieux(se) de savoir ce que je pourrais apprendre sur moi-même, en prenant conscience de la façon dont je réagissais à certaines pensées, sentiments ou sensations.	0	1	2	3	4
4. Je considérais mes pensées plus comme des évènements qui traversaient mon esprit que comme un reflet précis de ce que sont 'réellement' les choses.	0	1	2	3	4
5. J'étais curieux(se) de voir à quoi était affairé mon esprit d'un instant à l'autre.	0	1	2	3	4
6. J'étais curieux(se) à l'égard de chaque pensée et sentiment que j'éprouvais.	0	1	2	3	4
7. J'étais réceptif(ve) à l'idée d'observer tous pensées et sentiments désagréables sans chercher à les perturber.	0	1	2	3	4
8. J'étais plus investi(e) à simplement observer mes expériences lorsqu'elles survenaient, qu'à chercher à comprendre ce qu'elles pouvaient signifier.	0	1	2	3	4
9. J'ai abordé chaque expérience en essayant de l'accepter telle quelle, sans chercher à déterminer si elle était agréable ou désagréable.	0	1	2	3	4
10. Je demeurais curieux(se) à l'égard de la nature de chaque expérience qui survenait.	0	1	2	3	4
11. Je parvenais à être conscient(e) de mes pensées et de mes sentiments sans que je m'y attache outre mesure.	0	1	2	3	4
12. J'étais curieux(se) à l'égard de mes réactions aux évènements.	0	1	2	3	4
13. J'étais curieux(se) de savoir ce que je pourrais apprendre sur moi-même, en prenant simplement conscience de ce qui attirait mon attention.	0	1	2	3	4

German version

Bitte beantworten Sie jede dieser Aussagen indem Sie pro Reihe eine Antwortmöglichkeit auswählen.		**Stimmt gar nicht**	**Stimmt ein wenig**	**Stimmt teilweise**	**Stimmt ziemlich**	**Stimmt sehr**
TMS1	Ich habe mich selbst von meinen wechselnden Gedanken und Gefühlen getrennt wahrgenommen.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS2	Ich war mehr damit beschäftigt offen gegenüber meinen Erfahrungen zu sein, als sie zu kontrollieren oder zu verändern.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS3	Ich war gespannt, was ich womöglich über mich selber lerne, wenn ich mir darüber bewusst werde wie ich auf bestimmte Gedanken, Gefühle oder Empfindungen reagiere.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS4	Ich habe meine Gedanken mehr als Geschehnisse in meinem Geist wahrgenommen, anstatt als akkurate Wiederspiegelung der Art und Weise wie die Dinge „wirklich" sind.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS5	Ich war neugierig zu sehen, was meinen Geist zu verschiedenen Zeitpunkten beschäftigt.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS6	Ich war neugierig auf alle meine präsenten Gedanken und Gefühle.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS7	Ich war bereit dazu, unangenehme Gedanken und Gefühle wahrzunehmen ohne in diese einzugreifen.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS8	Mir lag mehr daran meine Erfahrungen bloß zu betrachten während sie entstanden, als herauszufinden was sie bedeuten könnten.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS9	Ich habe zunächst versucht jede Erfahrung zu akzeptieren, unabhängig davon ob sie angenehm oder unangenehm war.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS10	Ich blieb neugierig auf das Wesen jeder Erfahrung die nach und nach entstand.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS11	Ich war mir meiner Gedanken und Gefühle bewusst, ohne mich mit ihnen zu sehr zu identifizieren.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS12	Ich war neugierig auf meine Reaktion auf verschiedene Dinge.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
TMS13	Ich war neugierig was ich über mich selber lernen kann, wenn ich mir darüber bewusst werde, wodurch meine Aufmerksamkeit angezogen wird.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

AppendixS3: Situational Catastrophizing Scale
French version
Pour les questions suivantes, nous vous demandons de décrire les types de pensées et d'émotions que vous avez ressenties durant les procédures de douleur expérimentale. Vous trouverez ci-dessous treize énoncés décrivant différentes pensées et émotions qui peuvent être associées à la douleur. Veuillez indiquer, selon l'échelle ci-dessous, à quel point vous avez ressenti ces pensées et émotions durant cette séance de stimulation douloureuse.

0 – pas du tout	**1 – quelque peu**	**2 – de façon modérée**	**3 - beaucoup**	**4 – tout le temps**

1. _______ Je m'inquiétais de savoir à quel moment cela allait s'arrêter.

2. _______ J'avais peur que la douleur me submerge.

3. _______ Je sentais que je ne pouvais plus supporter la douleur.

4. _______ Je ne pouvais m'empêcher de penser à quel point cela me faisait mal.

5. _______ Je ne faisais que penser à quel point je voulais que cela s'arrête.

6. _______ Je pensais que les procédures étaient horribles.

German version
Anleitung: Bei den folgenden Fragen sind wir an der Art der Gedanken und Gefühle interessiert, den Sie während des Prozesses der Schmerzempfindung empfunden haben. Unten stehen verschiedene Aussagen die Unterschiedliche Gedanken und Gefühle beschreiben die mit Schmerz in Verbindung stehen. Bitte geben Sie mit den folgenden Skalen an, wie stark sie diese Gedanken und Gefühle während der Testdurchführung empfunden haben.

0 – gar nicht	**1 – kaum**	**2 – teilweise**	**3 – stark**	**4 – die ganze Zeit**

1._______ Ich habe mir Gedanken gemacht wann es zu Ende ist.

2._______ Ich dachte der Schmerz würde mich überwältigen.

3._______ Ich hatte das Gefühl ich könnte es nicht aushalten.

4._______ Ich konnte nicht aufhören daran zu denken wie sehr es schmerzte.

5._______ Ich habe mir fortwährend gewünscht, dass es fertig ist.

6._______ Ich fand, dass der Ablauf furchtbar war.

AppendixS4: Post-experiment manipulation checks

English version
1. **(i) During the heat stimulation session <u>preceding</u> the audio recording, did you notice any relationship between the colour of the fixation cross and the heat intensities that followed them?**

A. The green cue was associated with higher heat intensity than the purple cue.
B. The green cue was associated with lower heat intensity than the purple cue.
C. There were no differences in intensity between heat stimuli associated with the green cue and the purple cue
D. I don't know

(ii) How confident are you in your answer above?

1	2	3	4	5
Not confident at all				Fully confident

2. **Questions regarding the audio instructions:**

1	2	3	4	5	6	7
Not at all						Very much so

(i) Were the instructions clear to you? _____

During the pain testing session:

(ii) To what extent did you follow the provided instructions? _____

(iii) How easy for you was it to follow the provided instructions? _____

(iv) How successful do you think you were in applying the provided instructions? _____

French version

1. **(i) Durant la session de stimulation thermique <u>précédant</u> l'enregistrement audio, avez-vous remarqué quelconque relation entre la couleur de la croix de fixation et le degré de chaleur des stimulations qui les suivirent ?**

   A. La couleur verte était accompagnée par des chaleurs plus intenses que la couleur mauve.
   B. La couleur verte était accompagnée par des chaleurs moins intenses que la couleur mauve.
   C. Il n'y avait aucune différence entre les degrés de chaleur qui accompagnaient la couleur verte et la couleur mauve.
   D. Je ne sais pais

(ii) A quel point êtes-vous confiant(e) en votre réponse ci-dessus?

1	2	3	4	5
Pas confiant(e) du tout				Extrêmement confiant(e)

2. **Questions à propos de l'enregistrement audio**

1	2	3	4	5	6	7
Pas du tout						Complètement

(i) Est-ce que les instructions étaient claires pour vous? _____

Durant la séance de douleur expérimentale:

(ii) A quel point avez-vous suivi les instructions fournies? _____

(iii) A quel point était-il facile pour vous de suivre les instructions fournies? _____

(iv) A quel point pensez-vous avoir réussi à mettre en pratique les instructions fournies? _____

German version

1. **(i) Während der Hitzestimulation vor der Tonaufnahme, haben Sie da irgendeine Verbindung zwischen der Farbe der fixierten Kreuze und der Intensität der Hitze wahrgenommen die darauf folgten?**

E. Das grüne Signal war mit einer höheren Hitzeintensität assoziiert, als das lila Signal.
F. Das grüne Signal war mit einer niedrigeren Hitzeintensität assoziiert, als das lila Signal.
G. Es gab keinen Unterschied in zwischen der Hitzeintensität die mit dem grünen Signal und der die mit dem lila Signal assoziiert waren.
H. Ich weiß es nicht.

(ii) Wie überzeugt sind Sie von Ihrer oben angegebenen Antwort?

1	2	3	4	5
Gar nicht überzeugt				Gänzlich überzeugt

2. **Fragen bezüglich der Tonaufnahme:**

1	2	3	4	5	6	7
Gar nicht						Gänzlich

(v) Waren die Anweisungen für Sie klar? _____

Während des Durchgangs der Schmerztestung:

(vi) Zu welchem Grad haben Sie die gegebenen Anweisungen befolgt? _____

(vii) Wie einfach war es für Sie, die gegebenen Anweisungen zu befolgen? _____

(viii) Wie erfolgreiche glauben Sie bei der Umsetzung der gegebenen Anweisungen gewesen zu sein? _____

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