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## EDITED BY

Pavan Kumar,  
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Sciences University, India

## REVIEWED BY

Sebastian Gaston Alvarado,  
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Jacquelyn Tubbs,  
National Institutes of Health (NIH),  
United States

## \*CORRESPONDENCE

Cynthia Schuck-Paim  
✉ [cynthia.schuck@welfarefootprint.org](mailto:cynthia.schuck@welfarefootprint.org)

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# The pain echo chamber: how barren environments amplify pain in captive animals

Cynthia Schuck-Paim<sup>1\*</sup>, Wladimir J. Alonso<sup>1</sup>, Kate Hartcher<sup>1</sup>,  
Chiawen Chiang<sup>1,2</sup>, Patricia Alves Pereira<sup>1,3</sup>, Walter Veit<sup>4</sup>,  
Michael Mendl<sup>5</sup>, Christine J. Nicol<sup>6</sup> and Benjamin Lecorps<sup>5</sup>

<sup>1</sup>Welfare Footprint Institute, Winter Springs, FL, United States, <sup>2</sup>Department of Environmental Studies, New York University, New York, NY, United States, <sup>3</sup>Department of Biology, University of Crete, Crete, Greece, <sup>4</sup>Department of Philosophy, University of Reading, Reading, United Kingdom, <sup>5</sup>Bristol Veterinary School, University of Bristol, Bristol, United Kingdom, <sup>6</sup>Department of Pathobiology and Population Sciences, Royal Veterinary College, London, United Kingdom

Pain is not solely a function of tissue damage but can be strongly shaped by environmental context. Its perceived intensity, duration, and likelihood—the core features of affective experience—are modulated by factors including opportunities for behavioral engagement, control over environmental conditions, social environment, physical activity, sleep quality, maternal stress and pain early in life. All of these factors affect pain responses of captive animals, yet most welfare assessments and mitigation protocols treat pain as if it were context-invariant. Here, we review multiple lines of evidence indicating that environmental and rearing conditions modulate pain processing and healing in captive animals. We show that barren, confined environments disable multiple endogenous analgesic mechanisms, while simultaneously activating several neurobiological pathways that intensify nociceptive signaling and delay healing. Pain perception amplification and impaired healing are particularly likely when captivity is associated with intensive and barren environments. The implications of these findings are substantial. First, they highlight the need for animal welfare assessment models, and animal welfare research in general, to take environmental modulation of pain explicitly into account. Likewise, certification and regulatory frameworks must acknowledge that seemingly identical ailments or procedures can produce fundamentally different welfare experiences depending on the environment where they take place. Additionally, analgesic dosing protocols and laboratory-based pain models must be reevaluated for translational validity. More broadly, these findings challenge the acceptability of barren housing systems ubiquitous in farms, laboratories, and other settings. Given the substantial evidence that barren environments amplify and prolong painful states from common routine procedures and ailments, the transition to higher welfare housing systems becomes an ethical and scientific imperative.

## KEYWORDS

barren housing, endogenous analgesia, environmental enrichment, intensive animal farming, pain amplification, pain echo chamber, pain modulation, pain suppression

## Introduction

Pain is a conscious experience that emerges from adaptive signaling mechanisms, alerting organisms to actual or potential tissue damage and threats, and guiding protective behaviors. By its very nature, it is designed by natural selection to capture an organism's attention, serving to interrupt ongoing behavior and redirect focus toward the source of possible harm (Walters and Williams, 2019). This subjective experience emerges from complex interactions between ascending nociceptive signals—the detection and transmission of noxious stimuli—and descending modulatory influences, rather than being a simple reflection of actual tissue damage itself (Hoskin et al., 2019).

However, while individual differences in pain sensitivity are increasingly recognized (Nielsen et al., 2009; Ijichi et al., 2014; Lecorps et al., 2020), pain is largely treated as a fixed response to noxious stimuli, tissue damage and threat level—a signal that varies in intensity based on severity but that remains consistent regardless of an animal's environment or behavioral opportunities. While individual differences in pain sensitivity are increasingly recognized (Nielsen et al., 2009; Ijichi et al., 2014; Lecorps et al., 2020), the assumption of environmental invariance pervades multiple fields. For instance, animal welfare frameworks assign identical severity scores to identical painful conditions whether animals are housed in barren cages or enriched environments (Bracke et al., 2001; EFSA, 2012; Mellor, 2017) an inflamed hock is typically assumed to elicit the same pain and welfare impact independently of the housing and environment context in which it happens, and the same is the case for fractures, diseases, mutilations and other painful events. Likewise, veterinary analgesic protocols assume uniform dosing requirements regardless of housing conditions (Percie du Sert and Rice, 2014; Abboud et al., 2021); and laboratory pain models generalize findings from animals in restrictive housing to predict clinical efficacy in humans or other animals. Hence, whether an animal experiences inflammatory pain from arthritis, visceral pain from colic, neuropathic pain from nerve damage, or acute pain from a surgical procedure, the experience is assumed to be comparable regardless of whether the animal can engage in highly motivated behaviors, has social companions, or is under chronic physiological stress (Bracke et al., 2002; Welfare Quality<sup>®</sup> Consortium, 2009; Honess and Wolfensohn, 2010; Teng et al., 2018).

Still, mounting evidence challenges this assumption. Consider, for instance, the striking observation that chickens with experimentally-induced joint inflammation show complete suppression of pain behaviors when engaged in feeding after food deprivation—an effect entirely reversed by opioid antagonists (Gentle and Corr, 1995). Or that rodents housed in enriched environments require significantly less self-administered analgesia following surgery than those in barren cages (Pham et al., 2010). Or that in humans, distraction techniques can reduce pain perception by 30–45% (Morris et al., 2009; Moont et al., 2010; Verhoeven et al., 2011; Jensen et al., 2012), while chronic stress and sleep deprivation increase pain sensitivity by similar magnitudes (Jennings et al., 2014; Haack et al., 2020). These observations reveal that pain is not simply a reflection of nociceptive input, but rather emerges from complex interactions between ascending nociceptive signals and

multiple modulatory systems. Environmental factors such as housing, and their effects on neurophysiology, can change how these signals are processed, amplifying or suppressing the pain experience substantially. Moreover, many of the environmental and physiological factors that modulate pain perception also seem to influence healing capacity and recovery times (Gentle and Tilston, 1999).

Despite its fundamental importance, the environmental influence on pain processing has been largely overlooked in the animal welfare and veterinary sciences. This oversight has profound implications, as the welfare impact of any given ailment or source of harm cannot be assessed in isolation from environmental context. More troublingly, it suggests that animals in barren, restrictive environments may experience pain that is not merely unrelieved but biologically amplified beyond what would occur in more naturalistic settings. This is concerning for captive animals broadly, but particularly pronounced in intensive farming systems where barren environments converge with many additional stressors (Lecorps et al., 2021) that may further amplify pain pathways. While pain serves adaptive functions by promoting protective behaviors during healing, the environmental amplification documented here extends far beyond any protective benefit, particularly for chronic pain which frequently serves no adaptive function in captive settings (Walters, 2019).

In this review, we synthesize evidence from neuroscience, animal welfare and veterinary science, to examine how environmental factors modulate pain perception and healing in captive environments. We show that animals raised in barren environments are deprived of nearly all modulatory influences that enable endogenous pain suppression, while being simultaneously exposed to multiple pain-amplifying conditions.

We begin by briefly outlining the neurobiological mechanisms through which pain can be modulated, as understanding these pathways is crucial for recognizing how and why environmental factors can change the pain experience. We then examine common factors that trigger these mechanisms, and demonstrate how barren captive environments—particularly those seen in intensive farming systems—engage pain-amplifying and disable pain-suppressing pathways. This convergence, we argue, creates what we term a “Pain Echo Chamber”—an environment that fundamentally changes the phenomenology of pain itself, making many painful experiences more likely, more intense, and more prolonged than they would be otherwise.

## Mechanisms of environmental pain modulation

Multiple neurobiological systems mediate how environmental factors influence pain processing, operating across anatomical levels and temporal scales. They are summarized in Table 1. The following sections examine these mechanisms to enable understanding and predicting which environmental factors modulate pain and healing, the magnitude of potential effects, why experiences may vary across housing conditions, as well as allow generalization from specific observations to broader principles of pain modulation.

TABLE 1 Summary of pain-amplifying and pain-suppressing mechanisms.

Category	Pain effect	Mechanism	Brief description
Spinal (Bottom- Up)	Amplify	Central sensitization (wind-up)	Persistent nociceptive input increases spinal neuron excitability, amplifying pain.
		Structural rewiring (sprouting)	Chronic inflammation or injury leads to long-term spinal reorganization, leading to allodynia.
	Suppress	Gate control	Non-painful sensory input from movement or touch can inhibit nociceptive signaling at the spinal level.
Supra-spinal (Top- Down)	Amplify	Affective facilitation	Fear, anxiety or negative expectations heighten the emotional salience of pain and its perceived intensity.
	Suppress	Descending inhibition	Purposeful engagement or motivational states activate pathways that reduce nociceptive transmission.
		Cognitive distraction	Motivated activities divert attention away from pain processing.
Neuro-chemical	Amplify	Substance P & CGRP	Inflammatory sensitization, enhanced nociceptive signaling.
		BDNF-mediated central sensitization	Persistent stress or injury elevates BDNF, strengthening pain circuits and heightening sensitivity
		Serotonin influence	Depending on context, serotonergic signaling can facilitate or inhibit nociceptive transmission.
	Suppress	Endogenous opioids	Released during motivated behaviors, inhibit pain transmission.
		Oxytocin	Positive social contact triggers oxytocin release, reducing sensory and affective components of pain.
		Noradrenaline release	Behavioral engagement increases monoamine release, contributing to descending pain inhibition.
Neuro-Immune	Amplify	Pro-inflammatory cytokines	Inflammatory mediators sensitize nociceptors and promote prolonged pain responses.
		Pro-inflammatory microglial activation	Chronic stress locks microglia in a pro-inflammatory state that sustains central sensitization.
	Suppress	Anti-inflammatory cytokines	Anti-inflammatory mediators resolve nociceptor sensitization and support pain reduction.
		Reparative microglial activation	Microglia in a recovery-oriented state promote healing and reduce neuronal hyperexcitability.
Develop-mental	Amplify	Developmental programming	Early-life injury or stress alters nociceptor numbers and circuit wiring, heightening adult pain.
		Epigenetic modification	Chronic pain or stress induces epigenetic changes that promote long-term pain hypersensitivity.
		Gray matter changes	Prolonged pain leads to structural changes, weakening endogenous pain regulation.
	Suppress	Enrichment- induced neurogenesis	Enriched environments promote neurogenesis and support neural circuits involved in pain control.

## Peripheral and spinal ('bottom-up') pathways

Environmental factors first influence pain where signals enter the nervous system—at the spinal level. Gate control theory (Melzack and Wall, 1965) describes how non-painful sensory input can block pain transmission: when animals engage in movement or exploration, touch and vibration signals activate inhibitory neurons in the spinal cord that prevent nociceptive signals from reaching the brain—effectively “closing the gate” to pain. This explains why restricted movement removes a fundamental form of endogenous pain control. Where movement restriction is medically indicated—such as following orthopedic procedures—this loss of spinal-level pain modulation underscores the importance of optimizing other analgesic pathways. Conversely, repeated or intense pain, as caused by painful husbandry

procedures or common ailments, can cause central sensitization—spinal neurons become hyperexcitable and amplify all incoming signals (Latremoliere and Woolf, 2009). Through a process referred to as “wind-up”, each successive pain signal produces a larger response, progressively amplifying pain (Herrero et al., 2000). Eventually, even light touch can be perceived as painful (allodynia) and mild pain as severe (hyperalgesia) (Sandkühler, 2009). These functional changes can persist long after healing—a process documented across vertebrates, suggesting ancient evolutionary origins (Pinsker et al., 1973; Walters et al., 2023).

Beyond these functional changes, peripheral nerve injury arising, for example, from traumatic lesions (e.g., bodily mutilations) and chronic inflammation, can induce long-term structural reorganization within the spinal cord. First, following tissue damage, touch-sensing nerve fibers may sprout into areas normally reserved for nociceptive signals, creating new circuits

through which non-painful inputs trigger pain responses (Woolf et al., 1992). Second, sustained injury can change the balance of synapses, increasing excitatory connections and reducing inhibitory ones, resulting in a permanent bias toward pain transmission (Miletic and Miletic, 2008). These changes help maintain chronic pain even after the injury has healed.

## Supraspinal ('top-down') pathways

Pain is also modulated by descending supraspinal pathways that adjust nociceptive transmission according to cognitive, emotional, and motivational states (Millan, 2002). In mammals, for example, these pathways originate in midbrain regions and project to the spinal cord, where they modulate incoming pain (Fields, 2004). This system mediates diverse forms of analgesia—from pain suppression induced by acute fear (Fanselow and Baackes, 1982) to relief from rewarding experiences. While specific anatomical structures vary, functionally similar descending controls appear conserved across vertebrates and even invertebrates (Gentle, 2011; Sneddon, 2015; Khuong et al., 2019).

Critically, activation of descending modulation is activity-dependent. Passive exposure to the environment engages it weakly, whereas purposeful engagement—such as goal-directed movement or attentionally salient behavior—recruits endogenous analgesic systems more effectively (Tracey and Mantyh, 2007; Heinricher et al., 2009; Ossipov et al., 2010). Thus, environments that limit movement and engagement are likely to blunt activation of these pain-suppressing pathways (see 'Physical Exercise' section).

Cognitive and emotional appraisal also influence descending modulation. Perceived predictability or control over aversive events reduces stress-related pathology and pain responses, whereas unpredictability or uncontrollability promotes heightened pain sensitivity and persistent negative expectations (Weiss, 1972; Apkarian et al., 2005; Lecorps and Weary, 2024). Likewise, while acute fear may suppress pain, anxiety about future pain can amplify its salience (Neugebauer et al., 2004). Stress-induced elevations in corticosteroids further contribute to pain potentiation by acting on regions such as the amygdala, enhancing fear learning and the emotional dimension of pain (Korte, 2001). Glucocorticoid signaling is itself subject to epigenetic regulation: chronic stress can alter methylation of genes governing HPA axis function (Dion et al., 2022), potentially locking the stress-pain axis into a state of sustained activation even after the original stressor is removed.

Pain perception is also shaped by attentional resource allocation. When animals engage with competing stimuli, fewer cognitive resources remain available for pain processing, reducing pain perception depending on its intensity and the motivational salience of competing activity (Villemure and Bushnell, 2002; Sprenger et al., 2012). Conversely, where few competing demands exist, pain is more likely to dominate conscious experience. Still, when pain becomes sufficiently intense relative to other priorities, it can monopolize attention, disrupt responsiveness to external stimuli (Sneddon et al., 2003), impair memory formation (Moriarty et al., 2011) and disrupt most aspects of an animal's life (Weary 2014; Olsson et al., 2020). This principle also applies when multiple pain sources coexist. For example, lame chickens

showed higher thermal nociceptive thresholds than non-lame birds (Hothersall et al., 2014), suggesting that a dominant pain source can attenuate perception of additional pain. Alternatively, intense ongoing pain may recalibrate nociceptive sensitivity, rendering milder stimuli less salient (Lecorps and Weary, 2024).

Importantly, pain may also create a self-reinforcing dynamic, impairing the very cognitive capacities (attention, executive function, working memory) that enable top-down pain suppression. In humans, for example, chronic pain is associated with widespread cognitive deficits, which correlate with both pain duration and intensity (Rong et al., 2021; Bell et al., 2022; Chen et al., 2023; Patel et al., 2025). If similar impairments occur in animals experiencing pain in barren environments, they would progressively erode the capacity for attentional and cognitive pain modulation discussed above, contributing to an escalating cycle of pain amplification.

## Neurochemical mediators

Pain modulation ultimately depends on the actions of specific neurochemicals that either inhibit or facilitate nociceptive transmission. Among these, the endogenous opioid system is central to pain suppression. The body's natural opioids—including endorphins and enkephalins—produce powerful analgesia by binding to opioid receptors distributed throughout pain-processing pathways (Fields, 2004). These opioids inhibit the release of pro-nociceptive (pain-promoting) neurotransmitters, effectively blocking pain signals. Importantly, opioid receptor sensitivity is not fixed—chronic stress can downregulate these receptors, compromising the body's natural analgesic capacity (Corder et al., 2018). Endogenous opioid analgesia is highly conserved across vertebrates and invertebrates (Scharrer et al., 1988).

Monoaminergic pathways—involving neurotransmitters like noradrenaline and serotonin—provide additional pain modulation. Noradrenaline generally produces robust analgesia and mediates pain relief from behavioral engagement and cognitive distraction like grooming and environmental exploration (Ossipov et al., 2010). Serotonin itself can also directly modify gene expression through an epigenetic route: in the brain, serotonin is chemically attached to histone proteins, where it promotes a more permissive transcriptional state (Farrelly et al., 2019). This raises the possibility that serotonergic dysregulation in barren environments could alter pain-related gene expression in ways that outlast the original conditions.

In contrast, other neurochemicals consistently amplify pain. Neuropeptides like substance P and calcitonin gene-related peptides drive inflammatory responses and acute pain sensitization (Julius and Basbaum, 2001), while neurotrophins—particularly Brain-Derived Neurotrophic Factor (BDNF)—contribute to the long-term sensitization of pain circuits. Under persistent injury or stress, BDNF enhances synaptic efficiency in pain circuits, lowering their activation threshold and leading both to allodynia and hyperalgesia (Pezet and McMahon, 2006; Sandkühler, 2009). Notably, BDNF expression is itself subject to epigenetic regulation (Uchida et al., 2013), raising the possibility that stress- and pain-

driven increases in BDNF signaling are not merely transient but can become epigenetically consolidated.

Finally, oxytocin may lead to pain attenuation through social context. Released during positive social interactions like grooming or maternal care, oxytocin has both analgesic and anxiolytic effects, reducing the sensory and emotional components of pain (Neumann, 2008; Boll et al., 2018), an effect sometimes referred to as social analgesia (Mekhael et al., 2023). Animals deprived of positive social contact thus lose access to this endogenous analgesic pathway.

## Neuroimmune and inflammatory modulation

While the neural mechanisms previously described operate on a timescale of milliseconds to minutes, immune-inflammatory processes induce more persistent alterations in pain sensitivity lasting days to months. Pain involves bidirectional communication between the nervous and immune systems: inflammatory mediators sensitize the pain pathways, while neural signals modulate these inflammatory responses.

Following injury, immune cells release cytokines that modulate pain perception. Pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 sensitize nociceptors and amplify pain signals—an initially adaptive response that ensures protection of damaged tissue. Anti-inflammatory cytokines, including IL-10, IL-4, and TGF- $\beta$ , later resolve this sensitization by suppressing pro-inflammatory mediators (Scholz and Woolf, 2007).

Chronic stress shifts this balance toward persistent pro-inflammatory states that maintain pain long after healing. This disruption occurs partly through microglia, the nervous system's resident immune cells. These cells normally cycle between pro-inflammatory states (enhancing pain during acute injury) and anti-inflammatory states (promoting resolution). However, chronic stress locks microglia in pro-inflammatory activation (Inoue and Tsuda, 2018), bathing injury sites in inflammatory mediators that continuously sensitize nociceptors (Marchand et al., 2005). The result is a self-perpetuating cycle of pain: pain drives inflammation and inflammation maintains pain, with the system locked in a sensitized state (Ji et al., 2013).

## Developmental plasticity

Experiences during sensitive developmental periods can induce lasting changes that can affect pain processing throughout life, including structural changes in the brain itself. Chronic pain can induce such changes, including reduced gray matter volume in pain-modulating regions (Apkarian et al., 2004). Conversely, factors such as enrichment and exercise, can promote neurogenesis (May, 2008). Additionally, environmental deprivation and thwarting of behavioral motivations have been shown to lead to aberrant or maladaptive brain functions (Würbel, 2001). Underlying many of these changes are epigenetic modifications—molecular mechanisms that regulate gene expression without changing the DNA sequence. Chronic stress and persistent pain can induce DNA methylation and/or histone modification that act as “dimmer switches”,

increasing the expression of pro-nociceptive genes while suppressing anti-nociceptive ones (Descalzi et al., 2015). These epigenetic marks can lock the nervous system into a state of heightened pain sensitivity that may persist even if conditions improve. Direct evidence for pain-related epigenetic remodeling now exists in controlled models. In mice subjected to peripheral nerve injury, global DNA methylation in the prefrontal cortex decreased from 60% to 48% six months after injury, accompanied by chronic hypersensitivity and anxiety-like behavior (Tajerian et al., 2013). Critically, environmental enrichment reversed both the pain behaviors and the prefrontal methylation changes, and the degree of methylation recovery correlated with the magnitude of pain attenuation (Tajerian et al., 2013). At the gene-specific level, chronic neuropathic pain altered methylation of over 3,900 unique genes in the frontal cortex, affecting pathways involved in intracellular signaling, cell motility, and cytoskeletal structure (Topham et al., 2021). That these changes are genuinely epigenetic (rather than downstream correlates of pain) was confirmed by the finding that approximately one-third of them, spanning over 1,000 genes including genes with known pain-related function, were reversed when the DNA methylation pathway was targeted pharmacologically, concurrent with pain relief (Topham et al., 2021). Together, these two lines of evidence show that pain can be “memorized” in the brain through epigenetic mechanisms, and that this memory can be erased by improving the environment. These epigenetic effects have also been demonstrated in farmed animals. Piglets born to sows kept in barren environments during late gestation showed distinct DNA methylation profiles in the hippocampus, frontal cortex, and amygdala compared to piglets from enriched sows (Tatemoto et al., 2023). Consistent with this, differentially methylated regions associated with chronic social isolation stress were identified in the red blood cells of chickens across genetically distinct populations reared in different biomes (Pétille et al., 2020). Together, these findings indicate that the environmental modulation of pain discussed operates, at least in part, through epigenetic mechanisms that can sustain heightened pain sensitivity across time and generations, but that are potentially reversible when environmental conditions improve.

During neonatal and juvenile periods, the nervous system itself is also exceptionally plastic. Painful injuries or significant stress early in life can permanently change the trajectory of the pain circuit development, increasing the number of nociceptive nerve terminals, neurons with lower activation thresholds, and reorganizing synaptic connections (Schwaller and Fitzgerald, 2014). Functionally, early adversity can recalibrate stress and pain systems in ways that persist into adulthood, changing HPA-axis function, increasing anxiety-like behavior, and heightening nociceptive sensitivity, often leading to long-term hyperalgesia (Coffman et al., 2022). Critically, these adjustments are non-linear: across humans and animal models, repeated mild, controllable challenges are associated with more resilient later responses to stress and experimental pain, whereas both very low adversity (under-stimulation) and high or chronic adversity are linked to poorer regulation and increased pain sensitivity—a U-shaped “stress inoculation” or “toughening” pattern (Macri et al., 2009; Seery et al., 2013).

These developmental effects are not restricted to the directly exposed individual. For instance, maternal environmental enrichment before and during gestation in rats has been shown to reduce anxiety-like behaviors in the offspring (Zuena et al., 2016). Likewise, pre-reproductive maternal enrichment has been reported to increase maternal licking/grooming and nursing, leading to increased social interaction and reduced social avoidance in the next generation (Cutuli et al., 2019). Although these studies focus primarily on stress reactivity rather than nociception, changes in stress regulation are known to influence pain modulation, suggesting possible downstream, secondary effects on pain sensitivity (Bell and Hellmann, 2019).

The consequences of early or prenatal stress also depend on timing and severity: in primate models, brief, controllable stress exposures early in development enhanced later coping abilities, whereas prolonged or intense disruptions, such as maternal separation, increased vulnerability (Parker and Maestriperi, 2011). From an evolutionary perspective, such calibration may be adaptive when early adversity reliably signals a harsh environment, potentially favoring heightened vigilance or increased pain sensitivity (Veit and Browning, 2023). However, changes in pain sensitivity are not necessarily adaptive and may instead reflect side-effects of broader neuroendocrine plasticity. Moreover, early painful experiences may recalibrate reference points such that individuals develop a higher tolerance to pain, even if neural sensitization increases nociceptive processing. In captivity, this may give rise to a developmental mismatch if individuals shaped by barren or noxious early conditions remain hyper-reactive or hypersensitive despite later exposure to enriched environments.

## Healing modulation

Many factors that modulate pain perception also directly influence healing capacity, with both processes regulated by the same neuro-immune-endocrine systems. Healing is not passive but an active biological cascade that can be profoundly impaired by environmental stressors. Sustained activation of the HPA/I axis due to repeated or prolonged stress chronically elevates glucocorticoid hormones that directly impair healing by suppressing the immune system, dysregulating inflammation, and inhibiting cellular repair processes (Sapolsky et al., 2000; Glaser and Kiecolt-Glaser, 2005). As a result, injuries may not only feel more painful under chronic stress but also take longer to heal (Gentle and Hunter, 1993; Gentle and Tilston, 1999).

High levels of glucocorticoids also compromise immune function by inhibiting T-cell and macrophage proliferation, impairing pathogen clearance and debris removal. For example, pigs housed in barren, stressful environments exhibit slower viral clearance and more severe lung pathology than pigs in enriched environments (van Dixhoorn et al., 2016). Likewise, in chickens, stress-induced immunosuppression reduces responses to vaccination (Yunis et al., 2000; Cheema et al., 2003; Quinteiro-Filho et al., 2010), increases susceptibility to pathogens (Calefi et al., 2017; Hofmann et al., 2020) and delays wound healing (Quinteiro-Filho et al., 2010).

Beyond immunosuppression, chronic stress dysregulates the inflammatory cascade. Effective healing requires a rapid initial pro-inflammatory phase followed by an anti-inflammatory phase that resolves inflammation and promotes tissue rebuilding. Chronic stress prolongs the pro-inflammatory stage and delays the onset of the restorative phase (Glaser and Kiecolt-Glaser, 2005). Studies confirm this dysregulation, with chronically stressed animals showing significantly delayed wound closure compared to non-stressed controls (Padgett et al., 1998; Christian et al., 2006).

Finally, glucocorticoids directly inhibit cellular repair by suppressing fibroblast proliferation and the synthesis of collagen, essential for tissue rebuilding (Kruse et al., 1978). These mechanisms work together: chronically stressed animals experience enhanced pain perception, compromised immune defense, dysregulated inflammation, and inhibited tissue repair—making injury and disease more likely, more painful and slower to heal.

## Common factors triggering modulatory mechanisms

Having established the neurobiological mechanisms through which pain can be modulated, in this section we examine and illustrate common environmental and physiological factors that engage these pathways. This distinction serves two purposes. First, it acknowledges that individual factors rarely map onto single mechanisms, activating multiple pain-modulatory pathways simultaneously. Second, identifying common environmental factors provides targets for intervention, allowing the identification and modification of housing conditions, management practices, and experiences that can shape pain outcomes. Table 2 maps how these factors activate specific modulatory mechanisms.

## Opportunities for motivated behaviors and cognitive engagement

Active participation in motivated, goal-directed activities can activate top-down pathways that reduce pain perception. These activities typically involve highly motivated behaviors, such as nesting, feeding, foraging, and environmental exploration in general. For example, chickens with experimentally-induced arthritis showed pronounced limping, reduced weight-bearing on the affected leg, and decreased locomotor activity (Gentle and Corr, 1995). However, these impairments disappeared during feeding—an effect that scaled with hunger level. Birds deprived of food for 24 hours showed more complete suppression of limping than those deprived for only four hours, with normal locomotion persisting throughout feeding periods of up to thirty minutes (Gentle and Corr, 1995; Wylie and Gentle, 1998). In another set of experiments, chickens with induced arthritis in a familiar barren environment showed higher levels of cortisol, inflammation, and joint temperature than chickens placed in a novel pen (Gentle and

TABLE 2 Mapping of common factors in captive conditions to pain-modulatory mechanisms.

Factor	Effect on pain	Mechanism triggered
Opportunities for motivated behaviors and engagement	Suppression	Activates descending inhibition of nociceptive signals, stimulates endogenous opioid release, and induces attentional distraction that reduces pain processing.
Physical exercise and movement	Suppression	Induces endogenous opioid-mediated analgesia, reduces pro-inflammatory cytokines through improved circulation, and supports neuroplasticity that strengthens pain regulation.
Lack of physical exercise and movement (restriction/immobility)	Amplification	Reduces spinal gate control, sustains inflammatory sensitization, and increases baseline pain sensitivity.
Positive and stable social contact	Suppression	Triggers oxytocin-mediated analgesia and reduces stress-related activation of pain pathways.
Social isolation or unstable social conditions	Amplification	Promotes stress-induced central sensitization and delays healing through sustained hyperactivation of pain pathways.
Disrupted sleep and rest	Amplification	Increases pro-inflammatory cytokine activity and impairs descending pain inhibition, leading to heightened pain sensitivity and delayed healing.
Painful and stressful procedures in early life	Amplification	Induces central sensitization, structural rewiring, and long-term developmental programming of nociceptive pathways, including epigenetic modifications.
Maternal stress (additional factor)	Amplification	Changes offspring nociceptive and stress regulation via prenatal developmental programming, reducing endogenous pain suppression capacity.
Presence of control and environmental choice	Suppression	Engages descending modulation of pain through expectancy-based relief and supports adaptive neurochemical regulation of nociception.
Lack of control or unpredictable aversive exposure	Amplification	Sustains pro-inflammatory microglial activation and central sensitization through chronic stress-induced HPA/HPI overactivation.

Tilston, 1999; Gentle, 2001). A similar effect occurred during nesting: broody hens with induced joint pain showed normal weight-bearing and locomotion while building nests or brooding eggs, yet exhibited pronounced limping and one-legged standing when not engaged in these activities (Gentle, 2001). Critically, naloxone administration (a drug that blocks opioid receptors) reversed all pain suppression effects, indicating the involvement of endogenous opioids (Wylie and Gentle, 1998; Gentle, 2001).

This phenomenon extends across species. In cats, the temperature threshold for withdrawal responses to heat increases during feeding (51 °C during feeding versus 47 °C not feeding), indicating reduced pain sensitivity during behavioral engagement (Casey and Morrow, 1983). Similarly, rodents exploring novel environments showed reduced pain behaviors on formalin-injected paws (licking, biting, reduced weight-bearing), with effects mediated by changes in monoamines (Ford et al., 2008). In turn, opioid-mediated analgesia was found with prolonged exposure to a predator threat (Kavaliers and Colwell, 1991), while with short exposure (30 sec) to the threat, analgesia was insensitive to naloxone but blocked by a serotonin agonist, suggesting involvement of serotonergic pathways (Kavaliers and Colwell, 1991). Overall, the magnitude of pain suppression appears to scale with motivational salience, with highly motivated behaviors like nest-building and maternal care producing stronger analgesia (Bridges and Grimm, 1982; Gentle and Tilston, 1999). Additionally, some behavioral changes might reflect attentional reallocation. In cattle, oral distraction devices reduced struggle during freeze branding (Aitken et al., 2013). In humans, active task engagement was shown to reduce pain ratings in scenarios including a cold pressor task (Verhoeven et al., 2011) and during dressing in burn injury patients (Morris et al., 2009).

Overall, these findings indicate that behaviors that are motivated and engage attention activate multiple pain-

suppressing pathways, including opioid systems, serotonergic pathways, and cognitive-attentional processes, with their relative contributions depending on the salience of competing demands, the temporal dynamics of the experience and the intensity of pain.

## Physical exercise

Physical activity can suppress pain through both immediate and long-term mechanisms. Exercise induces analgesia through pathways including endogenous opioid release (Koltyn, 2000) and modulation of inflammatory responses. Regular joint movement maintains synovial fluid circulation and lymphatic drainage, reducing pro-inflammatory cytokine levels that would otherwise accumulate (Castrogiovanni et al., 2019). In humans, for example, increased physical activity improves pain ratings in a broad range of painful clinical conditions including low back pain, osteoarthritis, and fibromyalgia (Gowans et al., 2004; Smith and Grimmer-Somers, 2010). These effects have been shown to persist long after the exercise period (Naugle et al., 2012), likely reflecting continued circulation of endogenous opioids and anti-inflammatory factors.

Conversely, sedentary animals often develop chronic pain (reversible only through exercise-induced opioid release) (Bement and Sluka, 2005; Sluka et al., 2013), and those prevented from voluntary running show greater pain sensitivity (Stagg et al., 2011; Grace et al., 2016). In rodents, voluntary wheel running can reduce neuropathic pain behaviors and inflammation after sciatic nerve compression (Bertolini et al., 2011; Stagg et al., 2011). Lack of physical activity or prolonged immobility after an injury can also lead to delayed healing (Bement and Sluka, 2005; Keylock et al., 2008).

These effects of exercise appear conserved across vertebrates. In Atlantic salmon, swimming has been shown to promote neuroplasticity, enhance social cohesion, and reduce plasma

cortisol (Spiliopoulos et al., 2025). For example, active swimming following crowding stress accelerated the return of cortisol and metabolic indicators to baseline levels (Veiseth et al., 2006). Although these studies did not directly measure pain, the observed effects of exercise on stress reactivity, social behavior, and cognitive modulation point to its involvement in supraspinal (top-down) pathways with possible downstream effects on pain perception. Exercise may also build resilience against pain through neuroplastic changes. By elevating BDNF levels, exercise promotes neurogenesis (Siuciak et al., 1995; Bekinschtein et al., 2011), which in humans has been associated with reduced chronic pain (Vachon et al., 2013).

## Social contact

Evidence indicates that social context also modulates pain, yet its effects are complex and bidirectional, depending on factors including relationship quality and the nature of the interaction. For example, in rodents, socially enriched mice undergoing surgical cecal manipulation consumed less analgesic than mice in socially deprived environments (Pham et al., 2010). Accordingly, isolated mice show increased pain behaviors and delayed wound healing (Pyter et al., 2014). In lambs, the presence of a familiar partner reduced signs of pain such as rolling following a tail-docking procedure (Guesgen et al., 2014), whereas social isolation reduced mechanical pain thresholds (Clark et al., 2011).

In contrast, studies of disbudding in dairy calves have produced contradictory results: calves paired with conspecifics showed some signs of an improved ability to recover from disbudding in one study (Bučková et al., 2022), yet no social benefit was observed in another (Nogues et al., 2023). This variability may either reflect the influence of unmeasured contextual factors that determine whether social presence engages analgesic pathways, or the possibility that social buffering is not present in calves. Additionally, some animals may exhibit social withdrawal as an adaptive response to pain and inflammation (Gingerich et al., 2020; Zoltick et al., 2024), and forcing social contact in these cases may lead to aggression (Munsterhjelm et al., 2019) or loss of social status (Tansley et al., 2019). Finally, emotional contagion can create reciprocal welfare impacts, with pain in one individual reducing welfare in exposed conspecifics (Le Moëne and Larsson, 2025). The variability in outcomes indicates that implementing social housing requires careful consideration of species-specific behaviors, the stability of social hierarchies, and the severity of painful states.

Where beneficial effects occur, they appear mediated through oxytocin release and stress response modulation. While oxytocin's effects are most thoroughly documented in mammals, the oxytocin/vasotocin system and its role in social behavior is present across vertebrates (Akinrinade et al., 2023), suggesting potential parallel mechanisms for social pain modulation in other taxa. Epigenetic mechanisms also seem to underlie some of the effects mentioned. For example, maternal housing conditions during gestation have been shown to change DNA methylation in offspring brain regions governing emotionality and stress regulation (Tatemoto et al., 2023), suggesting that the consequences of social impoverishment may extend beyond the directly exposed individual.

## Disrupted sleep and rest

Sleep disruption, whether due to insufficient duration, poor quality, or irregular patterns, seems to be a potent amplifier of pain perception, likewise impairing healing. In rodents, for example, even partial sleep deprivation consistently increases sensitivity to thermal and mechanical pain and exacerbates the severity of inflammatory pain states (Lautenbacher et al., 2006; Haack et al., 2020). The hyperalgesic effect of suboptimal sleep is linked to both inflammatory and neural pain-modulating systems. Sleep is essential for regulating immune function, with disruption increasing pro-inflammatory cytokines and contributing to a state of systemic inflammation that lowers pain thresholds (Roehrs et al., 2006). Simultaneously, sleep deprivation can impair the efficacy of the brain's top-down analgesic pathways (e.g., endogenous opioids), compromising the ability to suppress pain (Przewłocka et al., 1986; Hakki Onen et al., 2001). This combination of enhanced pro-inflammatory signaling and impaired endogenous analgesia can lead to a state where pain is both more easily triggered and less effectively controlled.

These effects are also evident in other vertebrates. In Atlantic salmon aquaculture, continuous light protocols are routinely applied (Mota et al., 2024). Under these conditions, melatonin release is suppressed, as the pineal organ in salmonids depends on proper light-dark cycles for secretion (Iigo et al., 2007). Melatonin acts directly on the interrenal tissue (the functional equivalent of the adrenal gland) to inhibit *de novo* cortisol synthesis, functioning as an anti-stress signal (Azpeleta et al., 2023). Elevated glucocorticoids are well known for their immunosuppressive effects (Tort, 2011), whereas melatonin is critical for synchronizing immune cell activity and enhancing innate defenses (Cuesta et al., 2008; Esteban et al., 2013; Ren et al., 2015). Accordingly, salmon kept under continuous light exhibited delayed wound healing compared to 12:12 light-dark cycles or continuous darkness (Oldham, 2025).

## Painful experiences

Lasting changes in pain sensitivity that persist over life and across generations have been documented in multiple species and contexts. For example, exposure of gestating sows to an immune challenge has led to the downregulation of genes for key opioid receptors, impairing the offspring's natural pain-relief system (Rodriguez-Zas et al., 2024). This transgenerational downregulation of gene expression is consistent with epigenetic mediation, whereby maternal stress induces methylation changes in offspring that persist beyond the original challenge. Similarly, piglets of sows who experienced social mixing stress during mid-pregnancy showed significantly higher pain scores in response to tail-docking soon after birth, with average litter pain score correlated with the sow's cortisol levels during mid-gestation (Rutherford et al., 2009). These observations are in line with the hypothesis that maternal stress changes the developmental trajectory of nociceptive and immune regulation, leading to heightened pain responses and reduced resilience, possibly as an evolutionary adaptation to poor environments (Veit and Browning, 2023).

Similar effects are observed in fish. Although the effects of maternal stress on offspring pain sensitivity have not been directly investigated, maternal stress seems to affect offspring stress reactivity. In teleosts, cortisol is deposited into the oocyte and plays a critical role in embryonic development (Alsop and Vijayan, 2008). To prevent overexposure, ovarian follicles possess enzymatic mechanisms that restrict excessive cortisol incorporation into the eggs (Faught et al., 2016). However, whether this buffering capacity can compensate under chronic maternal stress remains unclear: high embryonic cortisol exposure can lead to dysregulated immune and stress function, and impaired tissue regeneration (Hartig et al., 2016), plausibly priming fish offspring for maladaptive responses to injury and pain.

Permanent changes in pain processing have also been demonstrated following painful procedures performed early in life. Rodents experiencing neonatal injury show substantially increased sensitivity to painful stimuli in adulthood (Ruda et al., 2000). Piglets castrated without analgesia displayed increased pain sensitivity weeks after the procedure (Hay et al., 2003), calves disbudded without pain relief showed heightened sensitivity to both thermal and mechanical stimuli months later (Adcock & Tucker, 2018) and, in sheep, female lambs that had been exposed to either tail-docking or a simulated infection during days 3–4 of their lives showed higher-levels of pain-related behavior when giving birth to their own first offspring (Clark et al., 2014). Beyond direct tissue damage, premature maternal separation has been associated with increased pain sensitivity in offspring across species (Vilela et al., 2017).

## Opportunities for control and environmental choice

The effects of environmental control and expectations on pain perception have been documented in various contexts (Habermann et al., 2025). In humans, control over pain offset or treatment onset shows the most consistent hypoalgesic effects. Recent work demonstrated that self-initiated treatment (via button press to reduce painful heat) led to lower pain ratings compared to externally initiated treatment, suggesting that control shifts expectations toward more effective treatment rather than modulating sensory precision (Habermann et al., 2025). In animals, research has primarily focused on how lack of control amplifies pain rather than how control might reduce it. Prolonged exposure to inescapable stressors—such as social instability, confinement, overcrowding, or persistent pain—often triggers hyperalgesia (Jennings et al., 2014). In rodents, chronic unpredictable stressors increased sensitivity to pain and prolonged recovery from injury (Maile et al., 2025). The inability to predict or control aversive events is linked with chronic activation of stress systems, leading to central sensitization and heightened pain perception.

While these studies indicate that removing control amplifies pain, environmental choice may provide animals with behavioral means to manage painful or inflammatory states through different mechanisms. For example, fish exposed to pathogens or inflammatory challenges, for example, actively seek warmer water

to induce behavioral fever (Huntingford et al., 2020). As ectotherms, fish cannot physiologically generate fever through internal metabolic processes as mammals do; instead, they must raise their body temperature behaviorally by moving to warmer areas. This thermoregulatory behavior enhances immune response and inhibits pathogen growth, allowing them to self-medicate through environmental navigation. While this represents management of the underlying inflammatory condition rather than direct pain modulation, it demonstrates how environmental choice enables animals to actively respond to painful or inflammatory states when such options are available. Additionally, environmental choice may support neurochemical systems involved in stress and pain regulation. For example, salmon reared in thermally enriched environments—where temperature gradients allowed thermal choice—exhibited higher levels of dopamine and serotonin (Sanhueza et al., 2018; Huntingford et al., 2020), neurotransmitters central to stress coping and pain modulation. When environmental choice is removed, animals lose both behavioral and neurochemical pathways for managing disease states and pain, potentially intensifying and prolonging it.

Expectations can also modulate responses to pain and generate placebo- and nocebo-like effects. This phenomenon is well-documented in humans (Bingel et al., 2011; Büchel et al., 2014; Hoskin et al., 2019) and may also exist in non-human animals (Nolan et al., 2012; Lecorps and Weary, 2024). For example, one study demonstrated placebo analgesia in rats that had learned to endure thermal stimuli to obtain a reward (Nolan et al., 2012). After experiencing pain relief from morphine during this task, the animals continued accessing the reward even when given saline injections instead, suggesting that anticipation of analgesia alone was sufficient to modulate their pain. Similarly, heifers trained using positive reinforcement to enter a headlock voluntarily showed reduced aversion to the headlock after it was associated with a mild subcutaneous injection, demonstrating that positive expectations engineered via positive training can reduce pain perception (Lomb et al., 2021).

Conversely, negative expectations may amplify pain through nocebo-like effects. For instance, animals that have experienced heightened pain may develop persistent negative expectations about painful stimuli, potentially maintaining hyperalgesia even after transfer to enriched environments. This learned anticipation of greater pain could represent an additional mechanism through which pain amplification persists beyond the immediate housing conditions, leading to a form of expectation-based sensitization.

## Systemic pain amplification under intensive conditions

While natural settings can offer a balance of factors that can either suppress or enhance pain perception, intensive and barren settings substantially reduce opportunities for the activation of the endogenous analgesic mechanisms discussed, while simultaneously promoting most of the pathways that heighten pain sensitivity and

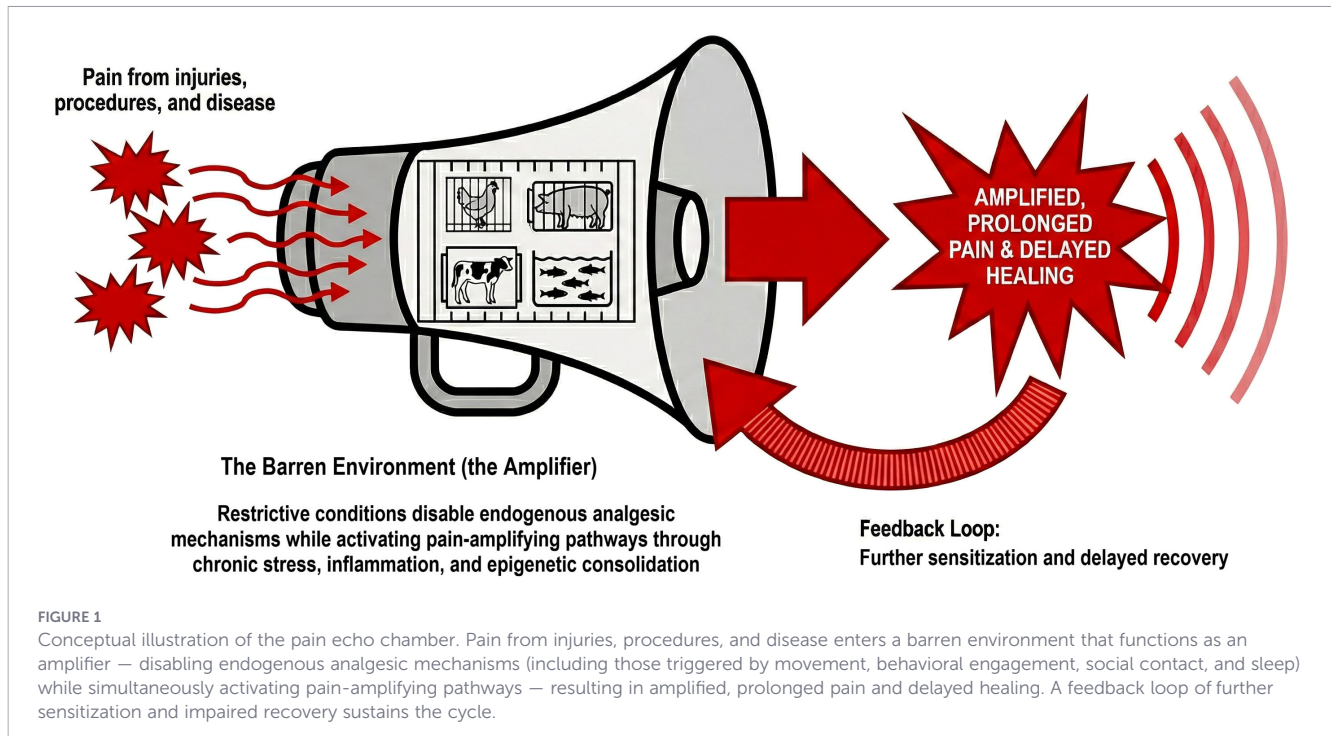
**TABLE 3** Mapping of pain-modulating factors to intensive rearing for caged egg-laying hens, breeding sows in crates, dairy calves, and salmon reared in recirculating aquaculture Systems, illustrating how common husbandry factors are predicted to inhibit pain-suppressing mechanisms while activating pathways known to amplify and prolong pain.

Conditions under conventional intensive farming	Laying hens in conventional cages	Breeding sows in crates	Dairy calves	Farmed salmon
Characterization: Stocking density, space availability	High stocking density; very limited floor and vertical space per bird (Lay et al., 2011; Freire and Cowling, 2013; Hemsworth, 2021)	Metal enclosures; insufficient to turn or change posture normally (Marchant-Forde, 2008; EFSA, 2022)	Individual hutches or small pens; limited space; high densities in group pens (Marcé et al., 2010; Hötzel et al., 2014; USDA, 2014)	Extremely high in hatcheries, limited horizontal/vertical swimming space (Stien et al., 2013)
Characterization: Barrenness	Barren cages, no perches, nests or substrate (Lay et al., 2011; Freire and Cowling, 2013; Hemsworth, 2021)	Concrete/slatted floors; no manipulable substrate (Marchant-Forde, 2008; EFSA, 2022)	Barren housing (Mandel et al., 2016), wire/solid floors with bedding	Barren tanks, no substrate/shelter; const flow & light (Reiser et al., 2025)
Opportunities for motivated behaviors and engagement	None: foraging, nesting, dust-bathing, exploration impossible (Lay et al., 2011; Freire and Cowling, 2013; Hemsworth, 2021)	None: nesting, foraging, exploration, wallowing prevented (Godyn et al., 2019; Mkwanzazi et al., 2019)	Often no opportunities for grazing or social & maternal interaction (Marcé et al., 2010; Hötzel et al., 2014; USDA, 2014; Costa et al., 2016)	Very limited: no shelter, substrate, current or temperature choice (Martins et al., 2012)
Physical exercise and movement	Walking, wing-flapping and other movements not possible (Lay et al., 2011; Freire and Cowling, 2013; Hemsworth, 2021)	Extreme confinement, no possibility of movement.	Kept in small pens; restricted locomotion (Costa et al., 2016; Mandel et al., 2016)	Abnormal swimming, natural and individual variation prevented (Martins et al., 2012)
Social contact	Small group sizes, competition for limited resources, inability to escape aggression (Lay et al., 2011; Freire and Cowling, 2013; Hemsworth, 2021)	Social isolation; abrupt weaning, mixing of unfamiliar piglets, inability to escape aggression (Marchant-Forde, 2008; EFSA, 2022).	Social isolation for young animals (individual housing), early maternal separation (Costa et al., 2016)	Fin-nipping, aggression, and establishment of rigid, stressful hierarchies (Martins et al., 2012)
Disrupted sleep and rest	Inability to roost, constant disruption from cage mates (Lay et al., 2011; Freire and Cowling, 2013; Hemsworth, 2021)	Crate prevents comfortable resting postures, constant noise (Marchant-Forde, 2008; EFSA, 2022).	Inadequate dry bedding & drafts/heat; disturbed lying bouts, constant lighting (Tucker et al., 2021)	Constant lighting, currents and noise; no quiescent zones (Bassi et al., 2022)
Painful and stressful procedures in early life	Beak-trimming, sexing, hatchery processing, immunization, transport (Hedlund et al., 2019)	Tail-docking; teeth clipping in some systems; injections; repeated handling (Sutherland, 2015; Ison et al., 2016; Adcock, 2021).	Maternal deprivation (Beaver et al., 2019), disbudding (Marquette et al., 2023a), castration (Marquette et al., 2023b), acute hunger after weaning (Weary et al., 2008)	Stressful hatchery and early rearing, repeated crowding/grading, transport/handling (Hoem and Tveten, 2023)
Maternal stress (additional factors)	Breeders in non-cage systems. Hens can be subject to repeated and sometimes aggressive attention from males. Bone fractures during laying (EFSA, 2023)	Chronic hunger, confinement, repeated farrowing; piglet removal, mixing (Marchant-Forde, 2008; EFSA, 2022).	Stress in gestation (heat, lameness), mastitis in lactation, peripartum practices (von Keyserlingk et al., 2009)	Crowding/handling, photoperiod/temperature manipulation, stripping of eggs/milt, spawning induction (Barton, 2000)
Control & Choice	No control over the environment or own behavior.			
Common painful conditions	Reduced bone strength and fractures (Sherwin et al., 2010), peritonitis, pecking wounds, vent and cloaca issues, footpad dermatitis (Lay et al., 2011; Freire and Cowling, 2013; Blatchford et al., 2016)	Lameness, pressure and gastric ulcers, mastitis-metritis, UTI, reproductive tract pain (Marchant-Forde, 2008; EFSA, 2022).	Navel infections, abdominal pain, sole, hock, joint & claw lesions, pneumonia, pleuritis (Thomsen et al., 2023; Roche et al., 2024)	Skeletal and jaw deformities, skin injuries, eye damage, gill pathologies, respiratory distress (Stien et al., 2013)

delay healing. These conditions are present in various captive settings, particularly those used for research animals, and in industrial animal farming, which typically involves the confinement of large numbers of animals at high stocking densities under barren conditions.

Overcrowding can amplify pain through most modulatory systems examined in this review. It often reduces the possibility of movement and physical exercise, hence the activation of afferent fibers that can inhibit nociceptive transmission, as well as exercise-

induced analgesia. It also reduces engagement in motivated activities such as exploration, that would normally activate descending analgesic pathways. It creates persistent social tension through the inability to establish stable hierarchies or escape agonistic encounters, degrades air quality through concentrated waste production, disrupts rest through constant disturbances, and generates chronic competition for resources. These factors engage, and sustain, the pathways that promote the chronic upregulation of the HPA/HPI axis, leading to a pro-inflammatory state that drives central



sensitization, resulting in allodynia and hyperalgesia. Impaired immune competence also delays healing and increases vulnerability to additional welfare challenges. Concurrently, barren conditions are similarly associated with the chronic deprivation of highly motivated behaviors, most of which can trigger the endogenous analgesic pathways discussed. Cognitive and sensory deprivation further remove attentional competition that would otherwise direct focus away from (mild and moderate) pain signals. Barren environments also remove opportunities to cope with these challenges, such as refuge areas and environmental choice.

These pain-amplifying conditions converge most severely in female breeders, who typically endure longer production cycles than animals raised for meat. They face repeated reproductive procedures including artificial insemination, pregnancy diagnosis, and parturition, alongside reproduction-related pathologies (e.g., mastitis, metritis, egg peritonitis). Chronic feed restriction, standard practice to ensure reproductive efficiency in breeders of fast-growing lines, also maintains these animals in states of persistent hunger (D'Eath et al., 2009), and the metabolic demands of reproduction create additional physiological stress. Housing systems for breeders often impose greater space restriction (e.g., gestation crates, farrowing crates, battery cages), and at least in the case of mammals repeated maternal separation adds psychological stress that further sensitizes pain pathways. The extreme conditions experienced by female breeders have cascading effects that go beyond pain amplification, creating intergenerational effects that amplify pain perception in the offspring too. Prenatal stress from mothers experiencing chronic pain, feed restriction, and confinement changes HPA axis development and nociceptive processing in the offspring. These effects compound when offspring themselves undergo painful procedures in early life and premature maternal separation, potentially establishing pain hypersensitivity for life.

Table 3 illustrates common husbandry practices associated with both pain amplification and suppression of endogenous analgesia in four farm animal groups: caged egg-laying hens, crated breeding sows, dairy calves and intensively reared Atlantic salmon. As shown in the table, multiple are the factors that act synergistically to create an environment of systemic pain amplification—a “Pain Echo Chamber”—where the likelihood, intensity and duration of painful experiences are magnified beyond what would be expected based on the underlying pathology (Figure 1).

## Implications and recommendations

The evidence that environmental context fundamentally modulates pain perception has profound consequences for welfare assessment and translational science. Welfare assessment frameworks that treat painful events as context-invariant risk systematically underestimate pain in barren conditions, and overestimating it under meaningfully enriched conditions. The solution requires either using housing-matched pain indicators—deriving intensity and duration estimates from animals in the specific system being assessed—or applying environmental correction factors when such data are unavailable. The latter will require investigating the magnitude of environmental modulation on pain salience and healing rates across species and conditions. Certification schemes and regulatory processes must also incorporate environmental modulation when evaluating severity. For instance, schemes that assign identical welfare scores to footpad dermatitis across all broiler systems will fail to account for how environmental context shapes this condition's impact. Different approaches could address this effect, including different outcome thresholds or welfare impact scales for different housing systems.

Until research can establish magnitude differences in the severity and duration of pain, a conservative approach is to derive pain indicators from the least enriched systems, so assessments capture worst-case scenarios where pain is maximal. Likewise, pain models built on barren laboratory housing may not accurately reflect drug efficacy or clinical relevance, requiring housing-based recalibration of analgesic testing and dosing. This aligns with calls to increase variability in animal housing and external validity of research findings (Voelkl et al., 2020).

The dynamic modulation of pain by environmental context bears practical implications. Critically, the provision of meaningful opportunities for behavioral engagement, agency, social interactions, and exercise must become a core feature of welfare standards. The emerging evidence that many environmentally driven changes in pain processing are mediated by epigenetic mechanisms, which are reversible with environmental improvement (Tajerian et al., 2013; Topham et al., 2021), also suggests that the benefits of enrichment extend beyond preventing future harm: they may actively reverse molecular changes that sustain heightened pain sensitivity in currently housed animals.

Importantly, enrichment should not be about maximizing stimulation, but rather choice and control. Some painful conditions will be compatible with social contact, movement, or cognitive engagement, while more severe states may adaptively motivate withdrawal, rest, and isolation (Proudfoot et al., 2014; Sundman et al., 2024). For instance, when movement restriction is medically necessary — such as during post-surgical recovery from orthopedic procedures — the temporary removal of exercise-induced analgesia makes it all the more important to optimize remaining modulatory pathways, including adequate pharmacological analgesia, comfortable resting conditions, and, where appropriate, choice of social contact.

This underscores why housing systems should provide animals with meaningful choices: opportunities to engage or withdraw, to move or rest, to seek social contact or isolation. Withholding such resources from animals, particularly those in chronic pain, constitutes a clear failure of adequate care. Additionally, enriched environments expand behavioral repertoires, allowing subtle behavioral deviations (e.g., reduced play, exploration) to signal emerging pain or disease earlier than in barren settings (Littin et al., 2008). This enhanced detectability is relevant in the context of early infectious disease detection (Nicol, 2025), and helps prevent painful conditions from progressing into chronic, amplified pain states.

These provisions are particularly relevant during early development, when nociceptive systems and stress–pain interactions are calibrated for life. Preventing sensitization caused by painful husbandry procedures and maternal or early-life stress is essential to avoid long-term hyperalgesic trajectories.

## Conclusion

Pain perception is not a fixed consequence of tissue damage but a dynamic phenomenon shaped by an animal's environment and

history. As demonstrated in this review, the same injury can produce profoundly different affective experiences depending on whether an animal can move, interact socially, engage in rewarding activities, rest properly, exercise control and access cognitive buffering. Barren housing, particularly under intensive conditions, systematically disables endogenous analgesic systems while simultaneously activating multiple pathways that amplify the perception of pain and delay healing. Pain in these conditions—what we describe as a Pain Echo Chamber—is not only unrelieved; it is amplified and prolonged beyond what the underlying pathology would otherwise induce. This is additionally concerning considering that pain can lead to longer-term affective disturbances, including depressive-like states such as negative mood and anhedonia, as shown in farm animals subjected to painful husbandry procedures or chronic injuries (Lecorps et al., 2021).

The consistency of findings across vertebrates, and even some invertebrates, suggests that environmental modulation of pain represents a fundamental biological principle rather than isolated phenomena. These findings challenge assumptions across animal welfare science, veterinary medicine, and translational research, suggesting that we may have systematically underestimated the pain experiences of animals in barren housing systems ubiquitous in farms, laboratories, and other captive settings. Given the evidence that barren and intensive conditions change the phenomenology of pain itself, the transition to higher welfare housing systems becomes an ethical and scientific imperative.

## Author contributions

CS-P: Conceptualization, Writing – review & editing, Writing – original draft, Methodology, Investigation. WA: Writing – original draft, Writing – review & editing. KH: Writing – original draft, Writing – review & editing. CC: Writing – original draft, Writing – review & editing. PP: Writing – review & editing, Writing – original draft. WV: Writing – original draft, Writing – review & editing. MM: Writing – original draft, Writing – review & editing. CN: Writing – original draft, Writing – review & editing. BL: Writing – review & editing, Writing – original draft.

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