Changes in Duration Perception in the Context of Pain

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Abstract

Duration perception refers to the perception of time intervals ranging from hundreds of milliseconds to several hours, and constitutes the foundation of numerous daily activities. Duration perception is influenced by a multitude of factors, such as arousal, attention, and motivation. Pain is a multidimensional psychological and physiological phenomenon comprising three components: sensory-discriminative, affective-motivational, and cognitive-evaluative. Recent research has demonstrated that duration perception can be altered in the context of pain. Research on duration perception in pain contexts primarily addresses three aspects: (1) duration perception of pain faces in healthy participants; (2) the effects of laboratory-induced pain on duration perception in healthy participants; and (3) changes in duration perception in clinical pain patients. Investigating alterations in duration perception within pain contexts can provide a novel perspective for understanding the mechanisms underlying the development and progression of pain, as well as the mechanisms of time perception.

Full Text

Adaptive Changes of Interval Timing in Pain Context

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Abstract

Interval timing refers to the perception of durations ranging from hundreds of milliseconds to several hours and forms the basis for numerous daily activities. This temporal perception is influenced by multiple factors, including arousal, attention, and motivation. Pain is a multidimensional psychological and physiological phenomenon comprising three components: sensory-discriminative, affective-motivational, and cognitive-evaluative. Recent research has demonstrated that interval timing is altered in pain contexts. Studies on interval timing in pain contexts primarily address three aspects: (1) time perception of pain faces in healthy subjects; (2) effects of experimentally induced pain on interval timing in healthy subjects; and (3) changes in interval timing among clinical pain patients. Investigating alterations in interval timing within pain contexts may provide novel perspectives for understanding both the mechanisms underlying pain development and the fundamental mechanisms of time perception itself.

Keywords: interval timing; pain faces; experimental pain; clinical pain; pacemaker-accumulator model

From grasping action rhythms in the tens of milliseconds to judging the passage of seconds, to experiencing the alternation of day and night and the changing of seasons—all fall within the scope of time perception. Interval timing represents a subcategory of time perception that specifically refers to the awareness of durations ranging from hundreds of milliseconds to several hours. This ability is crucial in daily life and influences individual behavioral choices (Buhusi & Meck, 2005). For instance, teachers must estimate when class will end to adjust their lecture pace, while chefs need to control cooking times to ensure dishes are prepared properly. However, interval timing is not an objective and accurate perception of elapsed time; rather, it is a highly subjective ability that depends on environmental context (Merchant, Harrington, & Meck, 2013). Among the various factors that affect interval timing are emotion, attention, and motivation (Lake, LaBar, & Meck, 2016). Changes in interval timing under specific circumstances follow certain patterns. For example, when confronted with angry faces (Doi & Shinohara, 2009; Fayolle & Droit-Volet, 2014; Gil & Droit-Volet, 2011; Gil, Niedenthal, & Droit-Volet, 2007), aversive stimuli (Gil & Droit-Volet, 2009, 2012), or fear-inducing stimuli (Buetti & Lleras, 2012; Grommet et al., 2011; Watts & Sharrock, 1984), people tend to overestimate durations. Conversely, when attention is diverted from temporal processing (Casini & Macar, 1997; Chen & O' Neill, 2001; Macar, Grondin, & Casini, 1994) or when motivation is strong (Gable & Poole, 2012; Soares, Atallah, & Paton, 2016), interval timing tends to be shortened.

Nearly everyone has experienced pain in real life. The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage." Pain is a multidimensional psychological and physiological phenomenon, with classic theories proposing that it comprises three components: sensory-discriminative, affective-motivational, and cognitive-evaluative (Melzack & Wall, 1965). In recent years, pain research has advanced to suggest that pain is not merely an individual experience but also possesses social attributes, as pain may be mutually influential between the individual experiencing pain and observers (Goubert et al., 2005). Some researchers have even called for incorporating a social dimension into new definitions of pain (Williams & Craig, 2016). Numerous studies have shown that pain can affect various cognitive functions, including attention, memory, and executive function (Berryman et al., 2014; Simons, Elman, & Borsook, 2014). Since pain sensation has a temporal dimension and manipulating interval timing can influence subjective pain experience (Pomares, Creac' h, Faillenot, Convers, & Peyron, 2011)—for example, misleadingly shortening the perceived duration of a noxious stimulus reduces reported pain intensity (Pomares et al., 2011)—we will explore the effects of pain on interval timing from three perspectives: pain faces, experimental pain, and clinical pain.

Although pain faces do not directly cause pain sensation in observers, recognizing pain expressions carries important evolutionary and social significance (Huang, Qiu, Liu, Li, & Huang, 2018; Williams, 2002). Neuroimaging studies have shown that observing others' pain faces activates brain regions similar to those activated during actual pain experiences, including the anterior cingulate cortex, insula, and amygdala (Cui, Abdelgabar, Keysers, & Gazzola, 2015). Therefore, this review includes pain face stimuli as a dimension for exploring pain' s influence on temporal perception, aiming to reveal how the social attributes of pain affect interval timing. Experimental pain is typically induced by brief exogenous noxious stimuli (mechanical, thermal, ice water, etc.) that cease when the stimulus is removed. Due to ethical constraints, such pain is relatively mild and predictable (Arntz & Hopmans, 1998; Crombez, Baeyens, & Eelen, 1994). Clinical pain, in contrast, is far more complex, often causing significant suffering, with some forms being intense and long-lasting. Clinical pain may persist even after the primary disease has been resolved and can induce neuroplastic changes in the brain. Consequently, we discuss experimental pain and clinical pain separately. Examining pain from the perspective of interval timing may help explain and predict behavioral changes in humans or animals under pain conditions, thereby deepening our understanding of the pain system's role. Additionally, this approach may provide new insights into the mechanisms underlying clinical pain development and inform novel pain interventions.

Furthermore, the perception of different durations involves distinct mechanisms. Droit-Volet (2013) proposed that sub-second timing primarily relies on sensory changes and represents an automatic processing procedure, whereas perceiving supra-second durations (e.g., several seconds to minutes) requires sustained attention directed at and maintained on the target, a process susceptible to attentional and working memory capacity limitations. This phenomenon is supported by neuroimaging evidence: sub-second timing primarily activates motor neural circuits such as the basal ganglia and cerebellum, which are considered closely related to the motor timing system, whereas supra-second timing more strongly activates cortical regions including the prefrontal and parietal cortex, associated with the cognitive timing system (Lewis & Miall, 2003; Mauk & Buonomano, 2004). Other researchers have suggested that when estimating durations under 5 seconds, relevant temporal information does not enter memory and represents a continuous perceptual process, whereas estimating longer intervals (e.g., tens of seconds to minutes) may involve memory encoding and retrieval, making the process more complex and warranting distinction between different duration perception processes (Fraisse, 1984). Most human studies require participants to perceive durations under 5 seconds, while animal studies have trained animals to perceive durations under 10 seconds. However, some studies have examined the effects of experimental and clinical pain on minute-scale interval timing and even the perception of time passage in daily life. In the following sections, we describe the effects of pain on both second-scale and minute-scale timing and discuss the differences between them.

2. Effects of Pain Faces on Interval Timing

2.1 Behavioral Studies on Pain Faces Affecting Interval Timing

Pain expressions are not a basic emotion category but rather a type of expression that simultaneously features characteristics of both sadness and anger (Kappesser & Williams, 2002). Functionally, pain expressions can signal a need for empathy, care, and help while also alerting observers to potentially harmful stimuli in the environment (Williams, 2002). Huang and colleagues employed a temporal bisection task to compare participants' perception of pain faces versus neutral faces and found that, regardless of whether face presentation durations were in the sub-second to supra-second range (400–1600 ms) or sub-second range (200–800 ms), participants were more likely to judge pain faces as "long" compared to neutral faces (Huang et al., 2018). The researchers fitted psychometric curves to participants' probability of "long" judgments as a function of face presentation duration to calculate the point of subjective equality (PSE)—the duration at which participants had a 50% probability of categorizing it as "long." The PSE for pain expressions was significantly lower than for neutral expressions, indicating that pain faces were perceived as longer in duration. The temporal bisection task is a classic paradigm in interval timing research (Church & Deluty, 1977; Thones & Oberfeld, 2015). In this task, participants first learn to discriminate between clearly distinct "short" and "long" durations. During testing, they are presented with a series of intermediate durations and must categorize each as either "short" or "long" (Church & Deluty, 1977; Thones & Oberfeld, 2015). Curve fitting yields the PSE parameter, with increases or decreases in PSE reflecting overall shortening or lengthening of interval timing within that time window (Church & Deluty, 1977).

Another study observed similar results. Using a temporal bisection task, researchers asked participants to make binary judgments about pain and neutral expressions presented for sub-second (200–800 ms) and supra-second (1400–2600 ms) durations. Participants more frequently judged both sub-second and supra-second pain expressions as "long" (黄顺航, 刘培朵, 李庆庆, 陈有国, 黄希庭, 2018). Additionally, the PSE for pain expressions decreased significantly, suggesting that subjective duration for pain faces was overestimated. This study also employed a temporal generalization task, requiring participants to perceive a series of stimulus durations (200–800 ms and 1400–2600 ms) and then judge whether presented stimuli were "equal" or "not equal" to a standard duration (500 ms for the 200–800 ms range; 2000 ms for the 1400–2600 ms range). Results showed that participants overestimated only sub-second pain faces, with no significant differences between supra-second pain and neutral faces (黄顺航等, 2018). Furthermore, participants rated pain faces as eliciting higher arousal than neutral faces. As previously noted, pain expressions share features with angry and sad expressions (Kappesser & Williams, 2002). Earlier studies using bisection tasks found that participants overestimated durations for high-arousal angry faces (Fayolle & Droit-Volet, 2014; Gil & Droit-Volet, 2011; Gil et al., 2007) but showed no significant timing changes for low-arousal sad faces (Fayolle & Droit-Volet, 2014) or even underestimation effects (G. Mioni et al., 2018). These findings suggest that overestimation of pain faces may share mechanisms similar to those for angry faces, with high arousal potentially mediating this process.

However, some researchers have reported different results. Ballotta and colleagues used a temporal production task, requiring participants to press a button to present pain or neutral faces for exactly 3 seconds while simultaneously judging face gender. They found that participants' keypress durations for pain faces were significantly longer than for neutral faces, indicating shortened interval timing for pain faces (Ballotta, Lui, Porro, Nichelli, & Benuzzi, 2018). This study also employed neuroimaging, observing that activation in the right middle temporal gyrus mediated pain face-induced changes in interval timing. These divergent results may be attributed to methodological differences: First, previous studies used temporal bisection tasks that require participants to perceive stimulus duration, retrieve reference memories for "short" and "long" standards, compare them in working memory, and make decisions—a process closely linked to working memory and decision-making. In contrast, Ballotta et al. used a temporal production task with minimal involvement of memory and decision processes (Gil & Droit-Volet, 2011). Second, their study employed a dual-task paradigm requiring participants to both time faces and judge gender, likely consuming cognitive resources. Third, they used a relatively long duration (3 seconds), whereas previous studies used shorter presentation times (<3 seconds), involving different cognitive components for different durations (Droit-Volet, 2013). These factors may collectively account for the discrepancy between Ballotta et al.' s findings and other studies.

2.2 Mechanisms Underlying Pain Face-Induced Temporal Perception Changes

Neuroimaging studies show that recognizing pain faces activates brain regions similar to those activated by pain signals, including the anterior cingulate cortex, insula, and amygdala (Cui et al., 2015). The anterior cingulate cortex plays a crucial role in attention maintenance and working memory (Dolcos et al., 2013), while insula and amygdala activation may mediate the temporal dilation induced by aversive stimuli (Dirnberger et al., 2012), suggesting overlapping neural mechanisms between pain face recognition and interval timing.

The pain system is closely related to arousal and attentional processes. Research indicates that when individuals are in high arousal states (as measured by skin conductance, heart rate, and subjective reports), their subjective interval timing tends to lengthen (Mella, Conty, & Pouthas, 2011; Schwarz, Winkler, & Sedlmeier, 2013). When attentional resources allocated to timing tasks decrease, interval timing tends to shorten (Casini & Macar, 1997; Chen & O' Neill, 2001; Macar et al., 1994), suggesting that arousal and attention are two key factors affecting interval timing. The classic pacemaker-accumulator (PA) model in interval timing integrates the roles of arousal and attention. The PA model proposes that humans and animals time intervals through an internal biological timing mechanism comprising a pacemaker, attentional switch, and accumulator (Gibbon, Church, & Meck, 1984). This model assumes that when attention is diverted from the timed stimulus, the attentional switch opens, interrupting the timing process and causing interval timing to shorten. Conversely, when physiological arousal increases, the operation rate of the internal timing mechanism accelerates, leading to lengthened interval timing. The PA model provides a theoretical framework for understanding the roles of arousal and attention in timing processes.

Participants in experiments typically rate pain faces as eliciting higher physiological arousal (Reicherts, Gerdes, Pauli, & Wieser, 2013). According to PA model assumptions, increased arousal when viewing pain faces may mediate temporal dilation. Attention may also mediate changes in interval timing for pain faces. Heathcote and colleagues used a dot-probe paradigm with reaction time as an index to examine attentional bias toward pain faces in healthy participants, finding that individuals with low attentional control showed attentional bias toward pain faces presented for longer than 1 second (Heathcote et al., 2015). Vervoort et al. employed eye-tracking technology and observed that healthy participants with low pain catastrophizing scores fixated on pain faces more quickly (Vervoort, Trost, Prkachin, & Mueller, 2013). In face timing tasks, participants must maintain attention on faces while perceiving duration. Within the PA model framework, when attention is diverted from the timed stimulus, timing is interrupted, causing interval timing to shorten. These studies suggest that during timing tasks, participants may orient attention more quickly to pain faces or maintain attention more effectively on them. Therefore, overestimation of pain faces may result from the combined effects of arousal and attention.

Additionally, the valence of pain faces (positive or negative) may mediate changes in interval timing. Pain expression stimuli are typically rated as having negative valence (Reicherts et al., 2013). Previous research has shown that when participants view negative stimuli, they estimate presentation durations as longer than for positive or neutral stimuli, regardless of whether they rate the negative pictures as high or low in arousal. Moreover, high-arousal positive pictures do not show overestimation effects (Angrilli, Cherubini, Pavese, &

Manfredini, 1997; Buetti & Lleras, 2012), suggesting that temporal dilation effects may be independent of arousal changes. However, these studies did not require participants to rate the positive or negative valence of pain faces, leaving a lack of direct evidence that pain face valence affects interval timing. Future research could explore this angle in greater depth.

3. Effects of Experimental Pain on Interval Timing

3.1 Effects of Experimental Pain on Second-Scale Timing

Pain expectation is closely related to emotion, with certain or uncertain pain expectations accompanied by anxiety or fear (Baliki & Apkarian, 2015; Karos et al., 2017). Previous studies have observed that fear emotions induce temporal dilation, and anxious individuals show lengthened interval timing when facing threats (Bar-Haim, Kerem, Lamy, & Zakay, 2010; Fayolle, Gil, & Droit-Volet, 2015; Tipples, 2011). As early as 1963, Hare used a verbal estimation task, asking healthy participants to estimate 5-second and 20-second intervals terminated by a painful electric shock to the fingertip. Results showed that when expecting the shock, participants overestimated both durations (Hare, 1963). Interviews with people who had experienced car accidents or robberies frequently revealed that they recalled time passing more slowly or even standing still during these critical situations (Tse, Intriligator, Rivest, & Cavanagh, 2004). Droit-Volet proposed that when facing threatening stimuli, individuals' defense mechanisms activate, putting them in a state of readiness for action (e.g., fleeing or avoidance) that is accompanied by temporal dilation (Droit-Volet, 2013). The temporal dilation induced by pain expectation may reflect that participants perceive pain as a type of threat.

Recent studies have examined changes in interval timing under experimental pain conditions in laboratory settings. Ogden and colleagues compared the effects of thermal pain and pain expectation on interval timing (Ogden, Moore, Redfern, & McGlone, 2015). This study first conditioned participants to associate neutral stimuli (geometric shapes) with thermal pain. Participants were then asked to estimate the presentation duration (200–1300 ms) of pain-conditioned neutral stimuli. Results showed that healthy participants estimated the duration of pain-conditioned neutral stimuli as longer. Additionally, participants in a state of thermal pain also showed overestimation of durations for unconditioned neutral stimuli, suggesting that both pain and pain expectation can lengthen interval timing. Rey and colleagues used a temporal bisection task to examine changes in sub-second interval timing in healthy participants under cold pressor pain. Participants placed their hands in 12°C cold water (pain condition) or 25°C room-temperature water (control condition) while a series of neutral stimuli (gray squares) were presented for durations ranging from 250–750 ms. Participants were required to perceive and categorize each stimulus duration as "long (750 ms)" or "short (250 ms)." The researchers fitted psychometric curves to the probability of "long" responses as a function of stimulus duration and found that participants in the cold pressor pain condition reported higher pain scores and showed increased probability of "long" judgments (Rey et al., 2017). The PSE derived from parameter fitting was significantly lower in the cold pressor condition, indicating that cold pressor pain lengthened interval timing. Moreover, PSE covaried with subjectively reported pain intensity: the stronger the subjective pain experience, the longer the subjective perception of neutral picture duration (Rey et al., 2017).

Similar results have been obtained in animal studies. Meck (1983) used a temporal bisection task to train rats to discriminate between 2-second and 8-second auditory stimuli by pressing different levers for food rewards. During testing, a series of intermediate durations (2–8 s) were presented while rats received 0.2 mA foot shocks. Results showed that under shock conditions, rats' psychometric curves shifted leftward and PSE decreased, indicating that foot shock induced temporal dilation. In tests conducted 1.5 hours after shock cessation, rats' psychometric curves shifted rightward and PSE increased, with animals more likely to judge durations as "short." However, the current intensity in Meck' s study was relatively weak, and nociceptive behaviors following shock administration were not systematically reported, making it unclear whether rats experienced nociceptive sensation. Nevertheless, this study helps us understand how electrically induced pain affects time perception.

3.2 Effects of Experimental Pain on Minute-Scale Timing

Other studies have compared the perception of longer durations (several minutes) under pain conditions in healthy participants. In a study by Thorn and Hansell (1993), healthy participants placed their hands in 7°C cold water (pain condition) or 35°C water (control condition) and were asked after 120 seconds how much time had passed. Participants in the pain condition showed significant underestimation of elapsed time. This finding was replicated by Hellstrom and Carlsson (1997) using the same procedure. Although participants in pain reported high arousal and low calmness and pleasure, they underestimated both 120-second and 300-second durations (Hellstrom & Carlsson, 1997). These results suggest that pain may influence minute-scale interval timing through alternative mechanisms.

3.3 Mechanisms Underlying Experimental Pain-Induced Temporal Perception Changes

Under laboratory conditions, researchers have consistently observed that both pain expectation and pain states lengthen participants' perception of durations ranging from hundreds of milliseconds to several seconds. Neuroimaging studies show that pain signals activate a series of cognitive-affective brain regions, including the anterior cingulate cortex and anterior insula, whose activity is thought to encode psychological aspects of pain (Wiech, 2016). As previously mentioned, the anterior cingulate cortex and insula may mediate the effects of emotional stimuli on interval timing (Dirnberger et al., 2012). Participants under experimental pain exhibit physiological signs of high arousal, such as increased blood pressure and heart rate (Roberts, Klatzkin, & Mechlin, 2015; Sambo, Howard, Kopelman, Williams, & Fotopoulou, 2010). Therefore, from the perspective of the PA model, the high arousal induced by pain may mediate temporal dilation.

Additionally, pain can capture attention and thereby affect cognitive tasks. Previous research has observed that acute experimental thermal pain significantly reduces accuracy in attention tasks (n-back paradigm) (Buhle & Wager, 2010), suggesting that pain and timing tasks may compete for attentional resources. The PA model assumes that when attention is diverted from the timed object, interval timing shortens (Droit-Volet, 2013; Lake et al., 2016). However, researchers have not observed this phenomenon in second-scale timing tasks. The perception of different durations involves distinct psychological mechanisms. For shorter durations, participants do not need to maintain attention on the timing object for extended periods, and the process is primarily influenced by arousal (Droit-Volet, 2013). In second-scale timing tasks, participants are affected by the high arousal induced by experimental pain, while pain’ s attention-capturing effects may not significantly impact interval timing, ultimately resulting in temporal dilation at this timescale. An important function of the pain system is to modify behavior. When an organism becomes aware of pain, it can rapidly become alert to the environment and avoid noxious stimuli, a process accompanied by anxiety (Baliki & Apkarian, 2015). Combined with previous theories, the temporal dilation of second-scale interval timing induced by pain and pain expectation may have evolutionary significance: nociceptive pain often has a clear external source, such as high temperature or mechanical stimulation. When expecting or experiencing pain, individuals rapidly enter an alert state that facilitates immediate effective action to avoid the source of harm and prevent further bodily injury, a state that may be accompanied by temporal dilation.

When the perceived duration extends to several minutes, however, participants under experimental pain 反而 perceive time as passing more quickly (Hellstrom & Carlsson, 1997; Thorn & Hansell, 1993). Perceiving minute-scale durations involves not only attention and arousal but also memory encoding and retrieval, engaging more cognitive components. Experimental pain may influence minute-scale interval timing through multiple pathways: (1) When perceiving longer durations, pain can capture attention, preventing participants from maintaining attention on the timed object for extended periods; (2) The high arousal state induced by experimental pain may only extend second-scale timing, with high arousal no longer playing a primary role when timing extends to several minutes; (3) In studies estimating minute-scale durations, participants must retrieve temporal information to make duration judgments, and pain can interfere with memory encoding and retrieval processes (Pitaes, Blais, Karoly, Okun, & Brewer, 2018), potentially causing errors in time estimation. However, only two studies have compared changes in minute-scale interval timing under pain conditions, and both used the same experimental procedure, limiting the interpretation of results.

It is important to note that experimental pain has limitations compared to real pain situations. First, pain intensity in experimental studies is typically set within a tolerable range, whereas real acute pain may be more intense. Additionally, participants in experimental pain studies are usually informed in advance that they will receive painful stimuli, and the disruptive effect of pain on attention tasks decreases when pain is predictable (Arntz & Hopmans, 1998; Crombez et al., 1994). In real situations, pain onset may be more difficult to predict. Therefore, the effects of experimental pain on time perception may be weaker than those in real acute pain scenarios.

4. Changes in Interval Timing Among Clinical Pain Patients

Approximately 15% of the world' s population suffers from chronic pain (Murray & Lopez, 2013). Chronic pain significantly reduces quality of life and is accompanied by various symptoms, including depression, insomnia, suicidal ideation, and decreased immune function (Baliki & Apkarian, 2015). Consequently, investigating psychological and cognitive changes in clinical pain patients has substantial applied value. Clinical pain patients exhibit impairments in psychological functions, such as reduced working memory capacity and attentional bias toward pain-related information, which affect cognitive activities (Simons et al., 2014). Additionally, some clinical pain patients complain that time passes more slowly in daily life (van Laarhoven, Schilderman, Verhagen, & Prins, 2011), suggesting that pathological pain may also affect interval timing. Several researchers have explored changes in interval timing among clinical pain patients. However, most relevant studies have focused on migraine patients, with a few examining time perception changes in advanced cancer patients who often experience severe pain. We have not found studies on interval timing in other types of clinical pain patients, so this section focuses primarily on research involving migraine and cancer patients. Since interval timing is influenced by emotion, examining changes in interval timing among clinical pain patients can reveal alterations in their cognitive or emotional states.

4.1 Effects of Clinical Pain on Second-Scale Timing

Anagnostou and Mitsikostas (2005) investigated the temporal discrimination ability of migraine patients for auditory stimuli separated by intervals of 30–100 ms (marked by two 5 ms pure tones). Compared to matched healthy controls, migraine patients showed no significant difference in discrimination accuracy, suggesting preserved ability to discriminate tens-of-milliseconds durations. The study also required migraine patients to perceive a series of durations (0.5, 1, 1.5, and 2 seconds) and judge whether they equaled 1 second (temporal generalization task) while measuring depressive symptoms using Hamilton' s Rating Scale for Depression. Although migraine patients performed similarly to healthy controls, those with depressive symptoms were more likely than healthy controls and non-depressed migraine patients to judge 0.5 seconds as 1 second. These findings suggest that depressive symptoms may mediate changes in interval timing among clinical pain patients.

Zhang et al. (2012) used a temporal reproduction task, requiring migraine patients (with headache duration of at least one year) to perceive neutral visual stimuli presented for 600 ms, 3 seconds, or 5 seconds and then reproduce the same duration via keypress. Results showed that migraine patients reproduced 600 ms durations as longer, but showed no significant differences from healthy controls when reproducing supra-second durations (3 and 5 seconds). The researchers speculated that migraine patients might have cerebellar functional changes that impair the motor timing system, manifesting as overestimation of sub-second durations. Vicario, Gulisano, Martino, and Rizzo (2014) observed similar results in a study using a temporal reproduction task with children suffering from migraine. Participants were asked to perceive neutral visual stimuli (black circles) presented for 1.5–1.9 seconds and then reproduce the same duration via keypress. The study found that children with migraine showed significantly lengthened interval timing. These two studies suggest that migraine patients tend to overestimate shorter durations (<2 seconds) while maintaining normal timing function for longer intervals.

Another series of studies examined changes in somatosensory temporal discrimination thresholds in migraine patients. Somatosensory temporal discrimination threshold is measured by presenting two consecutive mild electrical stimuli (at minimally detectable intensity) on the back of the hand and asking participants to temporally discriminate them. The minimum interval at which the two stimuli can be distinguished represents the somatosensory temporal discrimination threshold (Boran, Cengiz, & Bolay, 2016; Vuralli, Boran, Cengiz, Coskun, & Bolay, 2017; Vuralli, Evren Boran, Cengiz, Coskun, & Bolay, 2016). Vuralli et al. (2017) found that tension-type headache patients showed no significant difference in somatosensory temporal discrimination thresholds compared to normal individuals, whereas episodic migraine patients showed significantly elevated thresholds, though the study did not differentiate whether patients were in the headache phase. Boran et al. (2016) observed that episodic migraine patients during headache attacks had significantly higher temporal discrimination thresholds than during interictal periods and compared to healthy controls. Another study by Vuralli et al. (2016) found that chronic migraine patients showed elevated somatosensory temporal discrimination thresholds during both headache and interictal periods. According to the International Classification of Headache Disorders (3rd edition, ICHD-3), tension-type headache is characterized by no more than one day of headache per month, while chronic migraine is described as lasting more than three months with at least eight headache days per month, developing from tension-type headache. These studies suggest that the progression from tension-type headache to chronic migraine may be accompanied by changes in somatosensory temporal discrimination thresholds, and that such changes may serve as a biomarker for migraine patients.

4.2 Effects of Clinical Pain on Minute-Scale Timing

Isler, Solomon, Spielman, and Wittlieb-Verpoort (1987) examined changes in longer duration perception among headache patients. After respiratory biofeedback treatment lasting several minutes (13–42 minutes), the researchers asked headache patients to estimate the treatment duration and found that patients in the headache phase overestimated treatment duration more frequently than non-headache-phase patients and healthy controls. Additionally, when asked to read a text about "insomnia" and stopped after 180 seconds to estimate elapsed time, headache-phase patients overestimated the 180-second duration, whereas control groups of insomnia patients with headache history and healthy controls showed no such effect.

Anagnostou and Mitsikostas (2005) used the Time Awareness Questionnaire (TAW), which asks participants to recall how quickly time passes during daily activities (higher scores indicate faster subjective time passage), to examine migraine patients' perception of time passage in daily life. Although migraine patients did not differ from controls in TAW scores, depressed migraine patients scored significantly lower than non-depressed migraine patients, and TAW scores correlated negatively with depression scores—higher depression scores were associated with slower perceived time passage in daily activities (Anagnostou & Mitsikostas, 2005). Furthermore, van Laarhoven et al. (2011) compared time perception between asymptomatic patients and advanced cancer patients. Asymptomatic patients focused more on "future" events and held expectations for the future, whereas advanced cancer patients tended to focus attention on the "present moment,"perceiving present time as passing slowly or even standing still. Subjective time passage speed correlated inversely with personal distress scores—the greater the distress, the slower time was perceived to pass (van Laarhoven et al., 2011).

4.3 Mechanisms Underlying Clinical Pain-Induced Temporal Perception Changes

Chronic pain patients experience reduced working memory capacity, attentional bias toward pain information, and increased likelihood of depression and anxiety (Simons et al., 2014). Emotional state is an important factor influencing interval timing. For example, in temporal production tasks, depressed patients overproduce sub-second durations but show no differences from healthy controls for supra-second durations, whereas highly trait-anxious individuals show no significant differences (Giovanna Mioni, Stablum, Prunetti, & Grondin, 2016). In temporal reproduction tasks, highly trait-anxious individuals show underproduction of sub-second durations but normal reproduction of supra-second durations (Giovanna Mioni et al., 2016). Additionally, migraine patients have poor sleep quality, report more anxiety symptoms, and experience greater daytime fatigue (Engstrom et al., 2013; Engstrom, Hagen, Bjork, Stovner, & Sand, 2014), suggesting altered arousal levels. Overall, emotional changes in clinical pain patients may be an important factor affecting interval timing.

In current research, Zhang et al. (2012) and Vicario et al. (2014) both used temporal reproduction tasks and observed that migraine patients tend to overestimate sub-second durations but show no significant changes in timing for longer durations (>2 seconds). One explanation for this result is that the experimental paradigm influenced the outcome. In temporal reproduction tasks, participants must maintain the perceived duration in working memory and allocate attention to the reproduction process (Gil & Droit-Volet, 2011; Giovanna Mioni et al., 2016), and performance on temporal reproduction tasks correlates with working memory capacity (Baudouin, Vanneste, Isingrini, & Pouthas, 2006). In contrast, temporal production tasks involve output closely related to the operation rate of the internal timing mechanism and less related to memory and decision processes (Gil & Droit-Volet, 2011; Giovanna Mioni et al., 2016). Previous research has also observed inconsistent results between temporal reproduction and production tasks (Gil & Droit-Volet, 2011; Giovanna Mioni et al., 2016). Therefore, we speculate that the overestimation observed in migraine patients during temporal reproduction tasks may reflect impaired cognitive abilities (e.g., working memory, directed attention) rather than altered internal timing rates. Overall, research in this area remains limited, with single methodological approaches, and future studies should employ multiple interval timing measurement methods to obtain more comprehensive evidence.

Vuralli et al. (2017) and Boran et al. (2016) both observed that episodic migraine patients' somatosensory temporal discrimination thresholds increase during headache attacks but remain normal during interictal periods, whereas Vuralli et al. (2016) found that chronic migraine patients show consistently elevated thresholds. One explanation for these findings is that impaired dopaminergic system function mediates this effect. Both human and animal studies have observed dopaminergic system involvement in interval timing (Soares et al., 2016; Tomassini, Ruge, Galea, Penny, & Bestmann, 2016). Parkinson' s disease patients show normal somatosensory temporal discrimination thresholds in early disease stages but elevated thresholds after disease progression (Conte et al., 2016). A review analyzing studies from 1990 to 2017 on somatosensory temporal discrimination thresholds in Parkinson' s disease reported that threshold elevation correlates with disease duration and loss of dopaminergic neurons in the substantia nigra, and that these effects can be alleviated by dopamine-related treatments (Lee, Lee, Conte, & Berardelli, 2018), suggesting that elevated somatosensory temporal discrimination thresholds in Parkinson' s disease may result from dopaminergic dysfunction. Neuroimaging (Albrecht et al., 2016; DaSilva et al., 2017) and animal studies (Schwartz et al., 2014) have shown dopaminergic system dysfunction in chronic pain individuals, suggesting that the mechanism underlying elevated somatosensory temporal discrimination thresholds in migraine patients may be similar to that in Parkinson' s patients —both resulting from dopaminergic system impairment. However, this speculation is based solely on behavioral evidence, and direct neurophysiological evidence is lacking.

Some depressed clinical pain patients perceive daily time as passing more slowly or even standing still (Anagnostou & Mitsikostas, 2005; van Laarhoven et al., 2011). Depressed patients also frequently complain that time passes slowly in daily life (Droit-Volet, 2013; Wyrick & Wyrick, 1977). However, Droit-Volet (2013) noted that depressed patients' complaints about slow time passage may reflect their expression of daily life boredom—nothing can engage them, so attention focuses only on time passage—rather than altered neural mechanisms of time perception. In questionnaire surveys, researchers have observed that depressed patients focus more on past and present time, perceive present time as passing slowly, and ruminate on negative self-related thoughts while holding only negative views about the future (Wyrick & Wyrick, 1977). These results are similar to van Laarhoven et al.' s (2011) findings with advanced cancer patients, where those with higher distress levels also focused more on present time and less on future events. Therefore, the phenomenon of depressed clinical pain patients perceiving slow time passage may share mechanisms with depressed individuals' time perception, reflecting their negative and pessimistic mindset.

5. Conclusions and Future Directions

By reviewing research on changes in interval timing in pain contexts, we conclude that pain faces, pain expectation, and experimental pain all alter interval timing, and that interval timing is also changed in clinical pain patients. Within the theoretical framework of the PA model, the temporal dilation observed when viewing pain faces, expecting pain, or experiencing experimental pain may be related to increased arousal levels. The temporal dilation induced by pain faces, pain expectation, and experimental pain may reflect that individuals are in an alert, high-arousal state—a manifestation of activated defense mechanisms that supports the protective function of the pain system. In contrast, the depressive emotions accompanying clinical pain patients may cause them to perceive daily time as passing slowly. Additionally, the elevated somatosensory temporal discrimination thresholds in clinical patients reflect impairment in related neural circuits and may serve as a biomarker for certain types of clinical pain.

However, research on interval timing in clinical pain patients has several limitations. First, although current studies support changes in interval timing among clinical pain patients, the research has focused primarily on migraine patients, who cannot represent all types of clinical pain patients. Moreover, the predominant use of temporal reproduction tasks limits the interpretation of results. Second, although behavioral studies suggest that changes in somatosensory temporal discrimination thresholds may serve as a biomarker for migraine patients, neurophysiological evidence is lacking. Third, animal models and studies examining pain' s effects on interval timing are currently absent, limiting the acquisition of pharmacological and electrophysiological evidence from animal models.

Investigating changes in interval timing in pain contexts also has significant implications. First, an important question in pain research is how acute pain transitions to chronic pain. The temporal dilation observed under acute pain may reflect activation of defense mechanisms, whereas chronic pain patients do not show similar effects. This supports the distinction between acute and chronic pain from the perspective of interval timing. The elevated somatosensory temporal discrimination thresholds in chronic migraine patients suggest that neural circuits related to interval timing are involved in pain chronification, and interval timing may provide a new window for studying pain chronification. Second, all sensations and behaviors have a temporal dimension, and changes in interval timing under pain can explain behavioral alterations in pain contexts. For example, in delay discounting tasks, healthy participants under experimental pain prefer immediate small rewards over delayed large rewards (Koppel et al., 2017). From the perspective of interval timing, pain-induced temporal dilation may reduce the subjective value of delayed large rewards. Third, as pain is a subjective experience and interval timing can influence pain perception (Pomares et al., 2011), exploring the interaction between pain and time perception may help develop clinical or everyday strategies for coping with pain.

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