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The effects of experimental pain on episodic memory and its top-down modulation: a preregistered pooled analysis

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Abstract

Introduction: Pain can automatically interfere with ongoing cognitive processes such as attention and memory. The extent of pain's negative effects on cognitive functioning seems to depend on a balance between top-down and bottom-up factors.

Objectives: In this large, preregistered, pooled reanalysis of 8 studies, we investigated the robustness of the detrimental effect of acute pain on recognition memory and whether top-down mechanisms such as pain-related expectations or cognitions (pain-related fear, pain catastrophizing) modulate this effect.

Methods: Two hundred forty-seven healthy participants underwent similar experimental paradigms, including a visual categorization task with images randomly paired with (or without) concomitant painful stimulation and a subsequent unannounced recognition task. Recognition memory (ie, d', recollection, and familiarity) and categorization performance (ie, reaction time, accuracy) served as proxies for the effect of pain on cognitive performance.

Results: Acute painful stimulation significantly impaired recognition performance (d', familiarity). However, recognition performance was not significantly modulated by participants' expectations regarding the effect of pain on task performance or pain-related cognitions in this sample of healthy participants.

Conclusion: Our results corroborate the negative effects of pain on (visual) memory encoding reported in previous studies and reports of "memory problems" from patients with chronic pain. To characterize the role of bottom-up and top-down factors for the detrimental effects of pain, large-scale studies with more nuanced study designs are necessary. Future studies in patient cohorts must unravel the interaction of maladaptive pain-related cognitions and the often-reported impaired cognitive performance in chronic pain patients.

Keywords: Pain, Memory, Recognition, Expectation, Fear, Pain catastrophizing

1. Introduction

Pain inherently captures attention and impairs ongoing cognitive processes to protect individuals from potentially threatening situations. This so-called interruptive function of pain[13] has been demonstrated for acute, experimental,[7,17,18,28,29] and clinical pain[23,30] as well as chronic pain states.[20,31] Although most studies examining the effects of pain have focused on attention-related tasks,[30] we conducted a series of studies investigating the effects of pain on episodic memory[17,18,22,43,46] based on the observation that patients with chronic pain often report "poor memory"[27,33,41,45] and that such impairments have indeed been objectively demonstrated for different forms of memory, such as working memory and long-term memory.[27]

Episodic memory is a type of long-term declarative memory that involves the ability to learn, store, and retrieve information about personal experiences. By contrast, semantic memory

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involves memory for factual knowledge that has been learned, but for which the source of the original experience is usually not known. Once information is encoded and stored, it can be retrieved in different ways: Although recall is the process of retrieving previous events in the absence of a cue to help retrieve this information, recognition is characterized by a familiar feeling when a previously experienced event reappears. According to dual-process theories of episodic memory, 2 latent cognitive processes underlie recognition memory, namely, recollection (ie, recovering events and their context) and familiarity (ie, providing a sense of oldness).[56]

As described in the neurocognitive model of attention to pain,[26] the amount of attention captured by pain and its effect on simultaneously conducted cognitive tasks varies greatly and depends on a balance between bottom-up and top-down factors. Bottom-up factors comprise various stimulus characteristics, such as stimulus intensity,[9] novelty,[25] length,[47] or the painfully stimulated body site.[42,43] Top-down factors include, for instance, pain-related expectations,[17,46] pain catastrophizing,[54] or pain-related fear.[10] Given that patients with chronic pain often report cognitive impairment,[6,14,32,33] the role of such maladaptive cognitions as modulating top-down factors to the effects of pain on memory warrants further investigation.

We have conducted a series of studies investigating the effects of pain on episodic memory using various experimental pain types and modalities. These studies have now been pooled and reanalyzed to investigate the extent to which experimental pain stimuli impair visual object processing and memory encoding in healthy volunteers in a larger, heterogeneous sample. We included behavioral data from N = 247 healthy individuals from a total of 8 published[17,18,22,43,46] and unpublished studies (https://osf.io/k98sp/) that additionally assessed pain-related cognitions and used the same experimental paradigm with variation regarding, eg, stimulation site or pain modality. The modulatory influence of 3 clinically relevant top-down factors, ie, pain-related expectation, pain catastrophizing, and pain-related fear, was explored. We hypothesized that (1) experimentally induced pain would affect task performance, ie, alter reaction times during categorization and reduce recognition performance and (2) that the expectation of pain altering task performance would be positively associated with the observed pain-induced impairment in recognition memory, ie, stronger expectations of pain interfering with cognitive performance would be associated with lower recognition performance.

2. Materials and methods

2.1. Participants

Behavioral data from 8 studies performed at the University Hospital Essen and the University Medical Center Hamburg-Eppendorf, Germany with N = 272 healthy participants were combined. We pooled studies conducted in our laboratory that used the same memory paradigm including at least one pain condition and a pain-free control condition. **Table 1** provides details regarding the considered studies. Participants were informed that the study purpose was to investigate the interaction between the perception of neutral visual and painful stimuli. Final data analyses comprised 247 participants (all right-handed; 140 women and 107 men; age in years: 29.31 ± 10.51 (M ± SD); 18–71 years). 31 participants were excluded from the analyses for the following reasons: incidental MRI finding (n = 1), termination of the experiment due to strong movements in the MRI scanner (n = 1), falling asleep during MRI (n = 1), CES-D (Center for Epidemiologic Studies Depression) depression score >18 (n = 1),[22] high false-alarm rate (n = 1, outlier defined as >3 SD above mean false alarm rate), technical problems (n = 7), experiencing acute pain (n = 2), intake of pain medication (n = 1), awareness of the expectancy manipulation (n = 3), and non-compliance when providing pain ratings (n = 7). There is no information available for the remaining 6 participants. Participants reported normal or corrected-to-normal vision (including color vision) and no known history of neurological or psychiatric diseases, including no recurrent or chronic pain as assessed by self-report. No analgesic medication was taken on the day of the experiment. All studies were approved by the local Ethics Committees (Essen/Hamburg). Participants gave written informed consent, were free to withdraw from study participation anytime, and received monetary compensation.

2.2. Preregistration

This reanalysis was preregistered at the OSF (https://osf.io/k98sp/). Analyses reported in this article deviate from the preregistration regarding the exploratory research questions (ie, the effect of pain catastrophizing/pain anxiety on the expected effects of pain) because expectation of pain-cognition interaction did not modulate the effects of pain on memory performance (see results). Furthermore, this study focuses on the primary outcome (d') and its potential modulation by pain-related cognitions.

2.3. Experimental paradigm and procedures

All studies comprised similar experimental procedures that were performed on one study day. These procedures included informed consent, assessment of pain-related psychological traits, pain thresholds, and calibration of pain stimuli. Before the experimental task, pain-related expectations and pain-related fear were assessed in 6 out of 8 studies (**Table 1**). Afterwards, participants performed a visual categorization task (memory encoding) followed by a surprise recognition task. All studies considered in the reanalysis used adapted versions of the paradigm described in Forkmann et al. (2013) and were tailored to the particular research question. **Table 1** provides relevant specifics of each study (eg, number of trials, pain modalities, stimulation sites). Because of the brevity of this report, methods are only briefly described here. See **Table 1** as well as the published studies and methods of 2 unpublished studies (https://osf.io/k98sp/) for a detailed description.

2.3.1. Assessment of pain-related cognitions

Participants indicated on visual analogue scales (VAS) how pain would affect their task performance ("How do you expect pain to influence your task performance?" anchors left: "strong impairment," middle: "no change," right: "strong improvement"). Furthermore, participants' pain-related fear was assessed ("How fearful are you about the upcoming pain stimulation?" left: "not fearful at all," right: "extremely fearful"). In addition, participants completed the German version of the Pain Catastrophizing Scale[49] to investigate the relation with pain-related interference.

Expectations regarding the effects of pain on cognition were obtained in 6 studies (**Table 1**). Importantly, 5 studies examined genuine expectations, whereas expectancy was experimentally modulated in study 3 (for details regarding expectancy manipulation please refer to Sinke et al. (2016)).

Table 1

Overview of experimental details for each of the included studies.

Study	Reference	N*	Age (M ± SD)	N Male/ Female	Pain		Encoding task				Recognition task			Pretask ratings	Study type	DOI
					Modality	Stimulation site	Task duration (min)	No. of trials	No. of images per condition	Image/pain duration (s)	Task duration (min)	No. of trials	Image presentation duration (s)			
Study 1	Forkmann et al.,[18] 2013	24 (28)	26.50 ± 4.75	11/13	Heat (/Tone)	Arm†	16	60	20	2.5/2.5	14	120	1.5	—	Behaviour & fMRI	https://doi.org/10.1523/JNEUROSCI.2994-12.2013
Study 2	Forkmann et al.,[17] 2016	24 (24)	28.46 ± 4.80	12/12	Heat	Arm	25	80	40	2.5/2.5	40	160	1.5	Expectation	Behaviour & fMRI	https://onlinelibrary.wiley.com/doi/10.1002/ejp.822
Study 3	Sinke et al.,[46] 2016	42 (48)	25.23 ± 4.06	21/21	Heat	Arm	10	40	20	2.5/2.5	14	80	1.5	Expectation, fear	Behaviour & fMRI	https://onlinelibrary.wiley.com/doi/10.1002/ejp.928
Study 4	Schmidt et al.,[43] 2016	17 (20)	25.18 ± 4.57	8/9	Electrical	Hand‡/Face‡	10	60	20	2.5/2.5	12	120	1.5	Fear	Behaviour	https://doi.org/10.1016/j.neuroimage.2016.03.026
Study 5	Kleine-Borgmann et al.,[22] 2022	30 (39)	25.83 ± 8.85	7/23	Heat/ Visceral	Arm†/rectal†	25–30	63	21	3 × 2.5/ 12.5	25–30	126	2.5	Expectation, fear	Behaviour & fMRI	https://journals.lww.com/pain/Fulltext/2022/04000/Does_pain_modality_play_a_role_in_the_interruptive.13.aspx
Study 6	Unpublished	23 (23)§	26.65 ± 4.05	11/12	Electrical	Hand	25	60	20	2.5/2.5	30	120	1.5	Expectation, fear	Behaviour	https://osf.io/k98sp/
Study 7	Unpublished	28 (35)‖	24.93 ± 4.35	14/14	Electrical	Hand	25	60	30	2.5/2.5	30	120	1.5	Expectation, fear	Behaviour & fMRI	https://osf.io/k98sp/
Study 8	Unpublished	59 (61)#	39.63 ± 15.12	23/36	Electrical	Back‡/face‡	20	60	20	2.5/2.5	30	120	1.5	Expectation, fear	Behaviour	Unpublished, in preparation

* Number of participants analysed in the study. The number in brackets corresponds to the number of study participants before exclusion.

† Pain stimuli matched for unpleasantness.

‡ Pain stimuli matched for intensity.

§ In this study, 2 conditions of pain stimulation (simultaneous vs delayed) and 2 groups (immediate vs delayed recognition task) were compared. This reanalysis includes only the group with an immediate recognition task. Furthermore, the condition of delayed pain stimulation was excluded. For details on methods see OSF LINK.

‖ In this study, 2 groups (immediate vs delayed recognition task) were compared. This reanalysis includes only the group with an immediate recognition task. For details on methods, see OSF LINK.

The study sample comprised patients with chronic pain (migraine or back pain) and healthy participants. Only healthy participants were included in this reanalysis.

Table 2

Pooled analyses of categorization and recognition performance during painful and pain-free trials.

Outcome variables	N	Pain (M ± SD)	No pain (M ± SD)	β (±SE)	DF	t	P	d [95% CI]
Categorization task								
Categorization accuracy (%)	245	90.04 ± 9.00	90.30 ± 8.82	−0.005 ± 0.01	328.23	−0.96	0.341	0.08 [−0.09, 0.25]
Mean reaction time (ms)	245	1101.92 ± 232.37	1131.27 ± 233.88	−24.05 ± 20.10	7.20	−1.20	0.268	0.29 [−0.30, 0.89]
Recognition task								
Recognition performance (d')	245	0.90 ± 0.53	1.12 ± 0.54	−0.23 ± 0.07	6.56	−3.00	0.022	0.70 [0.15, 1.29]
Recollection parameter	197*	0.20 ± 0.16	0.22 ± 0.18	−0.02 ± 0.01	304.13	−1.71	0.089	0.16 [−0.02, 0.34]
Familiarity parameter	197*	0.64 ± 0.45	0.71 ± 0.52	−0.08 ± 0.03	309.31	−2.67	0.008	0.25 [0.06, 0.43]

* The 6-point confidence scale was used in 7 out of 8 studies. Thus, the analyses on recollection and familiarity are based on a lower number of observations.

2.3.2. Categorization task (memory encoding)

Participants performed a categorization task (memory encoding), in which neutral images depicting living or nonliving objects were presented (1) without painful stimulation or (2) with painful stimulation (thermal, electrical, or visceral pressure). Participants should indicate whether the image showed a living or nonliving object by button press as quickly as possible. The following information on task and stimulus details applies to all reanalysed studies. Trials were presented in a pseudorandomized order with no more than 3 consecutive trials of the same experimental condition. Image visibility was reduced to 33%. Two practice trials per condition were performed to familiarize participants with the task and ensure moderate to high pain perception. Details of the trial structure are given in **Figure 1A**. Trials were followed by pain intensity and/or unpleasantness ratings (VAS "How painful/unpleasant was the stimulus?" anchors: 0 = "not painful"/"not pleasant," 100 = "unbearably painful"/"unbearably unpleasant").

2.3.3. Recognition task

Subsequently, participants performed an unannounced recognition task, in which all pictures from the categorization task were shown intermixed with the same number of new images (lures) with 100% visibility and without painful stimulation. In studies 2 to 8, participants were asked to indicate on a 6-item scale ("surely old"—"surely new") whether they had seen a picture in the previous task by providing confidence ratings, whereas participants made "old/new" decisions in study 1. Details of the trial structure are given in **Figure 1B**; study specifics are listed in **Table 1**.

2.3.4. Behavioral outcome measures

2.3.4.1. Categorization—accuracy and reaction times

Categorization accuracy (% of correctly categorized images) was calculated separately for each experimental condition. Mean reaction time (RT) per condition was calculated for correctly classified images after removing outliers (RTs <200 ms or >2500 ms, and 3 SD above or below the individual mean).

2.3.4.2. Recognition—d'

The primary outcome was the discrimination index d', a measure of sensitivity or discriminability derived from signal detection theory,[48] that integrates hits (ie, correct classifications as old) and false alarms (ie, incorrect classifications as old). D′ was calculated for each condition separately to quantify the detrimental effect of painful stimulation on recognition memory using dichotomized confidence ratings ("old": answers "surely old," "probably old," "rather old"; "new": answers "rather new," "probably new," "surely new") and the formula d' = z(hit rate) – z(false alarm rate). Although higher d' values indicate better recognition memory (d' of 3 corresponds to almost perfect performance), a value of 0 indicates chance performance. Please note that the term "(detrimental) effect of pain," as used throughout the article, is not supposed to imply that the (negative) effects on cognitive functioning or task performance are specific to pain.

2.3.4.3. Recollection and familiarity

Recognition memory is assumed to be based on different processes—recollection and familiarity.[56] Recollection is characterized as remembering an item together with contextual information and is associated with high confidence. Familiarity can be associated with a wide range of confidence responses and entails the feeling of knowing an object, without specific contextual information.[12,56]

2.4. Pain stimuli

Pain (and visual) stimuli were controlled using the software Presentation (Presentation 16.3, Neurobehavioral Systems Inc, Berkley, CA). For study 5, the experimental task was conducted in Matlab (The MathWorks, Inc, Natick, MA) using external control through Psychtoolbox-3.[8]

Table 3

Pooled data for pain-related and task-related expectation, pain-related fear, and pain catastrophizing ratings.

Type of rating	No. of ratings	M ± SD	DF	t	P	d [95% CI]
Expectation of task interruption by pain (VAS −50 to 50)	230	−11.10 ± 16.50	229	−10.21	<0.001	−0.67 [−0.80, −0.54]
Pain-related fear (0–100)	299	38.83 ± 31.40	298	21.38	<0.001	1.24 [1.12, 1.35]
Pain catastrophizing (0–52)	246	12.52 ± 9.20	245	21.39	<0.001	1.36 [1.23, 1.49]

Note that the number of ratings (No. of ratings) and degrees of freedom (DF) differ for the different types of ratings due to the variation in study design (eg, 2 fear ratings per subject in studies with 2 pain conditions).
VAS, visual analogue scale.

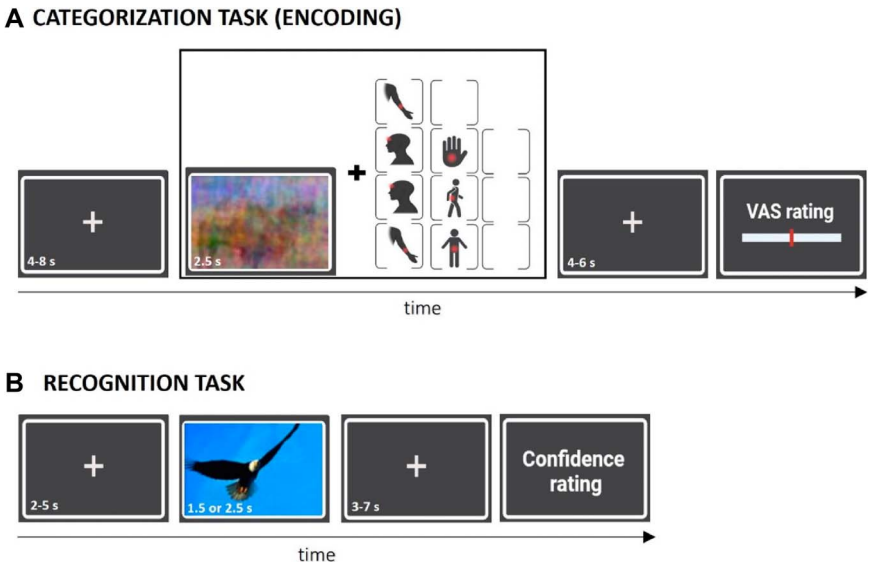

Figure 1. (A) Categorization task. Participants categorized neutral images of living or nonliving objects that were presented with reduced visibility (33%). A trial started with showing a white fixation cross for a variable duration of 4 to 8 seconds and was followed by an image presented for 2.5 seconds either alone or with concomitant pain stimuli. Pictograms represent the different types of pain stimuli used in the different studies. Following a white fixation cross for 4 to 6 seconds, a visual analogue scale was presented to rate stimulus intensity or stimulus unpleasantness. (B) Recognition task. Images from the categorization task (targets) and the same number of new images (lures) were presented with 100% visibility and without pain stimulation. A trial started with showing a white fixation cross for a variable duration of 2 to 5 seconds and was followed by the presentation of an image for 1.5 seconds (2.5 seconds in study 5) and another white fixation cross (3–7 seconds). Afterward, a rating was acquired using a 6-point confidence scale to indicate whether the images have been previously shown (surely old – surely new).

2.4.1. Heat pain stimuli

Studies 1 to 3 used contact heat pain applied through a thermal device (PATHWAY model CHEPS; Medoc, Ramat Yishai, Israel). The thermode (27-mm diameter) was attached to the left volar forearm using a strap. Stimulus duration was set to 2.5 seconds, except in study 5, in which heat stimuli with a plateau duration of 12.5 seconds were applied. Heat stimuli were triggered 470 milliseconds before the image onset (except in study 5) to ensure simultaneous perception of both stimulus types. For a detailed description of the pain stimuli, calibration and matching procedures see **Table 1**,[18,22] and Supplementary Table 1, http://links.lww.com/PR9/A238.

2.4.2. Visceral pressure pain stimuli

Visceral pressure pain was applied in study 5[22] using a pressure-controlled barostat system (modified ISOBAR 3 device; G & J Electronics, Ontario, Canada). A flexible catheter-affixed polyethylene bag of cylindrical shape (10-cm diameter) was

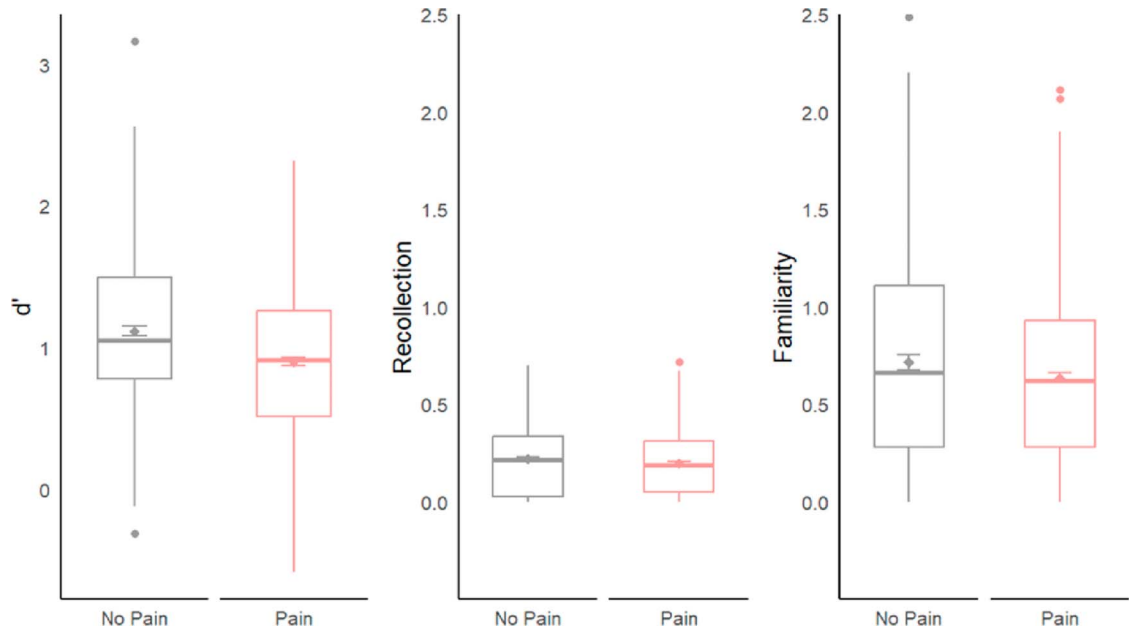

Figure 2. Pooled recognition performance with and without concomitant painful stimulation as assessed in the recognition task: d' values (left), recollection values (middle), and familiarity values (right) are given separately for both conditions. Box plots provide the distribution of d', recollection, and familiarity scores (including mean, median, and error bars = standard error of the mean). Dots represent outliers.

connected to a rectal tube with an outer diameter of 5 mm. After applying lubrication, the balloon was inserted into the rectum. The distal margin of the bag extended 5 cm beyond the anal verge. Rectal balloon distensions were administered intermittently, using phasic isobaric distentions, each lasting for 12.5 seconds at plateau. To achieve and maintain a constant level of pain unpleasantness, pressure stimuli were adjusted individually throughout the experiment.

2.4.3. Electrical pain stimuli

In Studies 4, 6, 7, and 8, electrical pain stimuli were applied. Electrical stimulators (Digitimer DS7A constant current stimulator, Hertfordshire, United Kingdom) were connected with surface electrodes of 5-mm diameter (Specialty Developments, Bexley, United Kingdom) and attached to the skin using medical tape. Electrodes were either attached to the left side of the forehead above the eyebrow and the lower back (study 8), the left side of the forehead and the left dorsal hand (study 4), or the left dorsal hand (study 6 and 7). In each trial, 82 single pulses were applied with a duration of 0.5 milliseconds and an interval of 30 milliseconds between pulses, resulting in a total painful stimulation of 2.5-second duration. Electrical stimuli were triggered simultaneously with image onset.

2.5. Visual stimuli

Neutral pictures showing that living or nonliving objects served as visual stimuli. Pictures were taken from the International Affective Picture System database[24] and purchasable picture CDs. Images presented in the categorization task were reduced in visibility (33%),[37,40] whereas images presented in the recognition task had full visibility. Please refer to Forkmann et al. (2013) for further details. For studies performed in the MRI scanner (Studies 1, 3, 4, 5, 7, 8), visual stimuli were back projected on a screen located behind the scanner that could be seen through a mirror attached to the head coil. All visual stimuli were presented for 2.5 seconds (categorization task) or 1.5 seconds (recognition task).

2.6. Statistical analysis

Linear mixed-effects models (LMM) were calculated to analyze all outcome measures using the lme4 package[4] in the R statistical software (R Core Team, [2022])[36] within the integrated development environment R Studio (Posit Team, [2023]).[35] Results with a $P < 0.05$ are considered statistically significant. The beta values ± standard errors (SE) and Cohen d as effect sizes are reported.

Analyses investigated potential differences between experimental conditions (*no pain* and *pain*) regarding categorization accuracy and RTs (categorization task) as well as d', recollection, and familiarity (recognition task). Note that data from different pain conditions were pooled, as we did not focus on potential differences between pain types but on the hypothesized negative effect of pain in general. Model calculations were performed individually for each outcome variable. All models were estimated according to the restricted maximum likelihood approach, and the best model was chosen according to the Akaike information criterion as indicated by the X^2 test for significance used for model comparison (see Supplementary Table 2, http://links.lww.com/PR9/A238). The following assumptions for conducting LMM analyses were tested and met: normality of residuals and homogeneity of variance. For the outcome categorization accuracy, data had to be log-transformed before LMM analysis to meet these assumptions.

Based on model fit, the final models for categorization hits, recollection, and familiarity included the fixed effect variable *condition*, with the factor levels *no pain* and *pain*. Random intercepts for both *study* and *subject* were included to account for the dependencies caused by repeated measures. The final model for d' and categorization RTs additionally included by-study random slopes. For all outcome variables, *age* and *gender* were included as covariates of no interest in the respective models to account for their potential modulatory effects.[19]

To test the assumption that expectation of pain-cognition interaction would be positively associated with the effect of pain on memory performance, ratings of *pain-related expectation* were added to the model as a covariate of interest. Further exploratory analyses included *pain-related fear* and *pain catastrophizing* as covariates of interest to investigate their potentially modulating influence on the effect of pain on memory performance. To this end, VAS ratings were transformed into numeric values (0–100 for pain-related fear) and the difference between the conditions *no pain* and *pain* were calculated for d'. Note that each study was powered to examine the effect of pain on task performance (d') but not the influence of pain-related cognitions upon this effect.

3. Results

3.1. Categorization task

Categorization accuracy was high and not altered by painful stimulation. Also, mean RT did not significantly differ between the conditions (see **Table 2** and Supplementary Figure 1, http://links.lww.com/PR9/A238).

3.2. Recognition task

Recognition performance (d') was significantly impaired for pictures previously paired with pain compared with those without pain with a medium to large effect size. Data from studies 3–8 allowed investigating recollection and familiarity. Recollection memory was not significantly impaired for pictures previously presented with painful stimulation. For the familiarity index, on the other hand, a significant small impairment for pictures previously paired with pain compared with those without pain was observed (see **Fig. 2** and **Table 2**, and Supplementary Figure 2, http://links.lww.com/PR9/A238 for differences of recognition performance delta d' [d'(no pain) − d'(pain)] for each study separately).

Overall, participants expected that pain would impair their performance in the categorization task (**Table 3**). We tested whether the effect of painful stimulation on recognition accuracy (ie, d') was modulated by participants' pain-related expectation or their cognitions (pain catastrophizing, pain-related fear). Analyses did not reveal any main effects or interactions of expectation (all $P > 0.30$; see Supplementary Figure 3, http://links.lww.com/PR9/A238), pain catastrophizing or pain-related fear (all $P > 0.08$).

4. Discussion

Different studies investigating the detrimental effects of acute pain on memory performance were pooled and reanalyzed to quantify the effects of experimental pain on visual categorization and recognition performance in a large sample of healthy volunteers. We further investigated the modulatory role of pain-related cognitions, such as expectations, pain catastrophizing, and fear of pain as previous smaller-scale studies have yielded mixed results. The analyses showed no pain-related impairment of categorization performance but

significantly reduced recognition performance (d') by pain with medium to large effect size.

Furthermore, we found a significant but small pain-induced impairment of familiarity-based recognition and no effect for recollection-based recognition. Pain-related expectations, fear of pain, and pain catastrophizing did not modulate the observed pain-induced memory impairment in the present sample.

4.1. Experimental pain affects memory performance

Reaction times during the categorization task were comparable across conditions. Although some previous studies observed impairment of performance speed during experimental pain,[3,18,52] others have shown facilitated reaction times during pain in cognitive tasks.[16,17,44] Those contradicting results are discussed in terms of pain-related attentional impairment and pain-induced arousal and increased alertness in those studies. However, because our large-scale analysis showed no effects of pain on reaction times, the effects previously reported in smaller studies could be due to behaviorally relevant shifts in the balance between bottom-up and top-down factors that led to stronger or weaker attentional binding to pain,[26] which we did not control for in the present reanalysis.

Moreover, as expected and observed before, categorization accuracy was not affected by pain. This might be explained by the low cognitive load of the task[29,53] as evident in the high categorization accuracy of more than 90% on average despite reduced picture visibility. Consistent with this and the neurocognitive model of attention to pain,[26] other studies have reported that pain-related impairment appears to depend on a task's cognitive demand[7,9,13,29] or perceptual load.[39]

Supporting this interpretation and consistent with our hypothesis, we observed a significant pain-related impairment in recognition performance (d'), indicating that the encoding of images was compromised by pain. This finding corroborates results from previous studies that observed impaired memory performance during both experimental[7,50,54] and chronic pain.[11,34] As previously discussed, due to its biological relevance and inherent warning function, the processing of pain captures task-relevant cognitive resources and therefore interferes with memory encoding. Although previous imaging studies suggest that neural activation in and connectivity between visual and memory-related brain areas are compromised when pain is applied during the encoding of images,[7,18,22] our study design does not allow to differentiate whether the observed pain-related memory deficits are a problem of feature processing and encoding or of feature retrieval. Future studies could address this question by comparing neural activation between pain stimulation during the encoding and recognition phases.

We further investigated whether the overall effect of pain on d' was driven by effects on one or both latent cognitive processes theorized to underlie recognition memory, namely, recollection and familiarity.[5] Our analyses indicate that familiarity-based recognition in particular appears to be impaired, whereas an adverse effect on recollection-based recognition was negligible. The formation of an ability to retrieve contextual information of an episode (or image) seems to be protective against the detrimental effect of pain on memory.

4.2. No modulation of the effect of pain on recognition performance by pain-related cognitions

We also tested the effects of pain-related expectations on memory impairment by pain, as expectations have been shown to affect the complex experience of pain in various ways.[2] Although effects of expectation have been observed in previous smaller scale studies,[17,46] this effect does not seem to be robust, as indicated by this large re-analysis. The here observed non-significant effect of expectation could be explained by the relatively low expectation ratings across the included studies, meaning that participants only expected a slight impairment of task performance by pain. Moreover, expectation ratings only referred to the categorization task whereas the recognition task was not known to the participants before the start of the experiment. Notably, studies in which expectations of pain-related impairment are higher, ie, when being manipulated by instructions,[46] showed the hypothesized positive correlation with actual impairment in task performance, even though expectations here again only referred to the categorization task.

Suitably, pain catastrophizing and pain-related fear did also not significantly affect pain-induced recognition impairment in our sample. Elevated maladaptive pain-related cognitions, such as fear of pain, pain catastrophizing, or hypervigilance, have been shown to lead to prioritization of pain processing and perception,[44,55] which in turn can negatively impact cognitive performance.[1,15,21,51,57] However, our data in healthy participants do not support a modulatory role of these top-down factors on pain-related memory impairment. These results have to be seen in light of the overall limited threat value of acute experimental pain in a safe laboratory environment and the relatively low variance of the considered pain-related cognitions in healthy individuals compared with patients with chronic pain. Moreover, the study design used here is not optimal for investigating the modulatory effects of pain-related cognitions. In addition, our study design did not test for a potential influence of bottom-up factors such as pain intensity or novelty nor for different aspects and levels of attentional load or attentional set.[25,26] Thus, more differentiated study designs are necessary to draw valid conclusions about the role of (and the interaction between) various factors in the detrimental effect of pain on cognition.

Negative pain-related cognitions are more prominent in patients with chronic pain. It should thus be investigated whether the relationship between maladaptive pain-related cognitions and the disruptive effect of pain is stronger in chronic pain samples than was observed in this healthy sample showing relatively little variation in those pain-related cognitions[38,58] and might increase the risk for development and maintenance.[55] Disentangling the relationship between altered cognitive functioning, eg, learning and memory mechanisms, and pain chronification or chronic pain, is warranted. Future studies thus need to investigate potentially relevant personality states and traits in patients with chronic pain and their association with alterations in cognitive functioning as a first step to reduce the functional impairment and increase patients' quality of life.

5. Conclusion

This large-scale reanalysis confirms the previously reported impairment of recognition memory by experimental pain in N = 247 healthy volunteers, consistent with the postulated detrimental effect of pain on memory encoding. Importantly, pain-related expectations, fear, and catastrophizing did not influence the effects of pain on memory performance in this large study sample. The heterogeneity across the included studies is a particular strength of this reanalysis, as it underscores the robustness and generalizability of the observed effects.

Future studies need to disentangle the relationship of maladaptive pain-related cognitions and the frequently reported cognitive impairment in chronic pain syndromes.

Disclosures

The authors have no conflict of interest to declare.

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Data and code availability: Data are available under https://osf.io/k98sp/. Code will be shared upon request from the first author.

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References

[1] Abelson E, Beckmann EA, Nahman-Averbuch H, King CD, Coghill RC, Mano KEJ. The interactive effect of pain catastrophizing and experimental pain on working memory performance as a function of cognitive load. J Pain 2022;23:5.
[2] Atlas LY, Wager TD. How expectations shape pain. Neurosci Lett 2012;520:140–8.
[3] Attridge N, Keogh E, Eccleston C. The effect of pain on task switching: pain reduces accuracy and increases reaction times across multiple switching paradigms. PAIN 2016;157:2179–93.
[4] Bates D, Mächler M, Bolker B, Walker S. Linear mixed-effects models using 'Eigen' and S4. R Package Version 4.0.2, 2014. Available at: https://cran.r-project.org/package=lme4. Accessed July 03, 2024.
[5] Bauch EM, Rausch VH, Bunzeck N. Pain anticipation recruits the mesolimbic system and differentially modulates subsequent recognition memory. Hum Brain Mapp 2014;35:4594–606.
[6] Berryman C, Stanton TR, Jane Bowering K, Tabor A, McFarlane A, Lorimer Moseley G. Evidence for working memory deficits in chronic pain: a systematic review and meta-analysis. PAIN 2013;154:1181–96.
[7] Bingel U, Rose M, Gläscher J, Büchel C. fMRI reveals how pain modulates visual object processing in the ventral visual stream. Neuron 2007;55:157–67.
[8] Brainard DH The psychophysics toolbox. Spat Vis 1997;10:433–6.
[9] Buhle J, Wager TD. Performance-dependent inhibition of pain by an executive working memory task. PAIN 2010;149:19–26.
[10] Crombez G, Vlaeyen JW, Heuts PH, Lysens R. Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. PAIN 1999;80:329–39.
[11] Dick BD, Verrier MJ, Harker TK, Rashiq S. Disruption of cognitive function in fibromyalgia syndrome. PAIN 2008;139:610–6.
[12] Dunn JC. How to fit models of recognition memory data using maximum likelihood. Int J Psychol Res 2010;3:140–9.
[13] Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychol Bull 1999;125:356–66.
[14] Eccleston C, Crombez G. Advancing psychological therapies for chronic pain. F1000Research 2017;6:461.
[15] Ellingson LD, Stegner AJ, Schwabacher IJ, Lindheimer JB, Cook DB. Catastrophizing interferes with cognitive modulation of pain in women with fibromyalgia. Pain Med 2018;19:2408–22.
[16] Erpelding N, Davis KD. Neural underpinnings of behavioural strategies that prioritize either cognitive task performance or pain. PAIN 2013;154:2060–71.
[17] Forkmann K, Schmidt K, Schultz H, Sommer T, Bingel U. Experimental pain impairs recognition memory irrespective of pain predictability. Eur J Pain 2016;20:977–88.
[18] Forkmann K, Wiech K, Ritter C, Sommer T, Rose M, Bingel U. Pain-specific modulation of hippocampal activity and functional connectivity during visual encoding. J Neurosci 2013;33:2571–81.
[19] Graves LV, Moreno CC, Seewald M, Holden HM, van Etten EJ, Uttarwar V, McDonald CR, Delano-Wood L, Bondi MW, Woods SP, Delis DC, Gilbert PE. Effects of age and gender on recall and recognition discriminability. Arch Clin Neuropsychol 2017;32:972–9.
[20] Grisart J, van der Linden M, Bastin C. The contribution of recollection and familiarity to recognition memory performance in chronic pain patients. Behav Res Ther 2007;45:1077–84.
[21] Grisart JM, van der Linden M. Conscious and automatic uses of memory in chronic pain patients. PAIN 2001;94:305–13.
[22] Kleine-Borgmann J, Schmidt K, Scharmach K, Zunhammer M, Elsenbruch S, Bingel U, Forkmann K. Does pain modality play a role in the interruptive function of acute visceral compared with somatic pain? PAIN 2022;163:735–44.
[23] Kuhajda MC, Thorn BE, Klinger MR, Rubin NJ. The effect of headache pain on attention (encoding) and memory (recognition). PAIN 2002;97:213–21.
[24] Lang PJ, Bradley MM, Cuthbert BN. International affective picture system (IAPS): Instruction manual and affective ratings, technical report A-8. Gainesville: The Center for Research in Psychophysiology, University of Florida, 2008.
[25] Legrain V, Perchet C, García-Larrea L. Involuntary orienting of attention to nociceptive events: neural and behavioral signatures. J Neurophysiol 2009;102:2423–34.
[26] Legrain V, Damme SV, Eccleston C, Davis KD, Seminowicz DA, Crombez G. A neurocognitive model of attention to pain: behavioral and neuroimaging evidence. PAIN 2009;144:230–2.
[27] Mazza S, Frot M, Rey AE. A comprehensive literature review of chronic pain and memory. Prog Neuropsychopharmacol Biol Psychiatry 2018;87:183–92.
[28] Moore DJ, Eccleston C, Keogh E. Cognitive load selectively influences the interruptive effect of pain on attention. PAIN 2017;158:2035–41.
[29] Moore DJ, Keogh E, Eccleston C. The interruptive effect of pain on attention. Q J Exp Psychol (Hove) 2012;65:565–86.
[30] Moore DJ, Keogh E, Eccleston C. Headache impairs attentional performance. PAIN 2013;154:1840–5.
[31] Moore DJ, Meints SM, Lazaridou A, Johnson D, Franceschelli O, Cornelius M, Schreiber K, Edwards RR. The effect of induced and chronic pain on attention. J Pain 2019;20:1353–61.
[32] Moriarty O, Finn DP. Cognition and pain. Curr Opin Support Palliat Care 2014;8:130–6.
[33] Oosterman JM, Derksen LC, van Wijck AJM, Veldhuijzen DS, Kessels RPC. Memory functions in chronic pain: examining contributions of attention and age to test performance. Clin J Pain 2011;27:70–5.
[34] Park DC, Glass JM, Minear M, Crofford LJ. Cognitive function in fibromyalgia patients. Arthritis Rheum 2001;44:2125–33.
[35] Posit Team. RStudio: integrated development environment for R. Posit software. Boston, MA: PBC; 2023. Available at: http://www.posit.co/. Accessed July 03, 2024.
[36] R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2021. Available at: https://www.R-project.org/. Accessed July 03, 2024.
[37] Rainer G, Augath M, Trinath T, Logothetis NK. Nonmonotonic noise tuning of BOLD fMRI signal to natural images in the visual cortex of the anesthetized monkey. Curr Biol CB 2001;11:846–54.
[38] Rogers AH, Farris SG. A meta-analysis of the associations of elements of the fear-avoidance model of chronic pain with negative affect, depression, anxiety, pain-related disability and pain intensity. Eur J Pain 2022;26:1611–35.
[39] Romero YR, Straube T, Nitsch A, Miltner WHR, Weiss T. Interaction between stimulus intensity and perceptual load in the attentional control of pain. PAIN 2013;154:135–40.
[40] Rose M, Schmid C, Winzen A, Sommer T, Büchel C. The functional and temporal characteristics of top-down modulation in visual selection. Cereb Cortex 2005;15:1290–8.
[41] Schmidt J, Fritz M, Weisbrod M. Relevance of neurocognition in chronic pain syndrome: a systematic and methodical approach. J Clin Exp Neuropsychol 2023;45:874–89.
[42] Schmidt K, Forkmann K, Schultz H, Gratz M, Bitz A, Wiech K, Bingel U. Enhanced neural reinstatement for evoked facial pain compared with evoked hand pain. J Pain 2019;20:1057–69.
[43] Schmidt K, Forkmann K, Sinke C, Gratz M, Bitz A, Bingel U. The differential effect of trigeminal vs. peripheral pain stimulation on visual processing and memory encoding is influenced by pain-related fear. Neuroimage 2016;134:386–95.
[44] Schmidt K, Schunke O, Forkmann K, Bingel U. Enhanced short-term sensitization of facial compared with limb heat pain. J Pain 2015;16:781–90.
[45] Schnurr RF, MacDonald MR. Memory complaints in chronic pain. Clin J Pain 1995;11:103–11.

[46] Sinke C, Forkmann K, Schmidt K, Wiech K, Bingel U. Expectations impact short-term memory through changes in connectivity between attention- and task-related brain regions. Cortex 2016;78:1–14.
[47] Sinke C, Schmidt K, Forkmann K, Bingel U. Phasic and tonic pain differentially impact the interruptive function of pain. PLoS One 2015;10: e0118363.
[48] Stanislaw H, Todorov N. Calculation of signal detection theory measures. Behav Res Methods Instrum Comput 1999;31:137–49.
[49] Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. Psychol Assess 1995;7:524–32.
[50] Tiemann L, Schulz E, Gross J, Ploner M. Gamma oscillations as a neuronal correlate of the attentional effects of pain. PAIN 2010;150:302–8.
[51] van Damme S, Crombez G, Eccleston C. Retarded disengagement from pain cues: the effects of pain catastrophizing and pain expectancy. PAIN 2002;100:111–8.
[52] van Damme S, Lorenz J, Eccleston C, Koster EHW, De Clercq A, Crombez G. Fear-conditioned cues of impending pain facilitate attentional engagement. Neurophysiol Clin 2004;34:33–9.
[53] van Ryckeghem DML, Crombez G, Eccleston C, Liefooghe B, van Damme S. The interruptive effect of pain in a multitask environment: an experimental investigation. J Pain 2012;13:131–8.
[54] Vancleef LMG, Peters ML. Pain catastrophizing, but not injury/illness sensitivity or anxiety sensitivity, enhances attentional interference by pain. J Pain 2006;7:23–30.
[55] Vlaeyen JWS, Crombez G, Linton SJ. The fear-avoidance model of pain. PAIN 2016;157:1588–9.
[56] Yonelinas AP. Components of episodic memory: the contribution of recollection and familiarity. Philos Trans R Soc Lond B Biol Sci 2001;356: 1363–74.
[57] Ysidron DW, France JL, Himawan LK, France CR. Pain resilience, pain catastrophizing, and executive functioning: performance on a short-term memory task during simultaneous ischemic pain. J Behav Med 2021;44: 104–10.
[58] Zale EL, Lange KL, Fields SA, Ditre JW. The relation between pain-related fear and disability: a meta-analysis. J Pain 2013;14:1019–30.