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ORIGINAL RESEARCH

Working Memory Load-Dependent Cortical Mechanism of Distraction Analgesia in Healthy Individuals: An fNIRS Study

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Purpose: As a central element of executive function, working memory (WM) contributes to pain regulation by balancing cognitive resources between goal-directed attention and attention captured by nociceptive stimuli. Although WM load influences pain perception, its modulatory mechanism remains to be explored, particularly functional network interactions among pain-related brain regions during distraction. This study aims to investigate the effect of different-load WM tasks on pain perception via behavioral measures and functional near-infrared spectroscopy (fNIRS) data, and to explore the underlying cortical neural mechanism.

Patients and Methods: Thirty-five healthy participants completed experiments under synchronized fNIRS. In the first part, participants completed a laser stimuli pain-rating task. In the second part, a 2 × 2 within-subject design was used to assess the distraction effect on pain perception. Participants performed an n-back task during two WM loads: high load (2-back) and low load (0-back), while receiving stimuli (with or without laser stimuli) to their right hand. All participants completed trials in five experimental conditions: pain task, 0-back task, 2-back task, 0-back with pain task, and 2-back with pain task. Pain intensity ratings and cognitive performance (accuracy and reaction time) were recorded.

Results: High load WM significantly reduced both the perceived pain intensity and nociceptive neural activation in the primary sensorimotor cortex (SM1) and secondary somatosensory cortex (S2). In contrast to n-back task, n-back with pain task showed a significant reduction in functional connectivity between brain regions within the high load group, including RS2-anterior prefrontal cortex (aPFC), RSM1-right dorsolateral prefrontal cortex (RDLPFC), RSM1-aPFC, and LSM1-aPFC.

Conclusion: This study provides evidence for load-dependent cortical mechanism of distraction analgesia in healthy individuals. We conclude that distraction analgesia effect of WM may result from suppression of sensorimotor cortical activity and decoupling of pain-processing networks.

Keywords: distraction analgesia, working memory, pain, cortical mechanism, functional near-infrared spectroscopy

Introduction

As an important cognitive factor, attention plays an important role in pain processing.[1–5] Distraction through synchronized activities may reduce pain sensitivity. According to the theory of limited cognitive resources in psychology,[6] the two-way interaction between pain and cognition can be explained from "bottom-up" and "top-down" mechanisms.[7] Acute pain triggers bottom-up automated attentional capture through thalamo-insular pathways that prioritize cognitive resources to initiate protective responses. Experimental evidence has shown that nociceptive input can divert attention from the current task to the nociceptive stimuli. Irrelevant nociceptive stimuli interfere with cognitive performance by competing for limited attentional resources.[8] Simultaneously, top-down attention control can modulate pain perception through distraction. When attention is allocated to the tasks without pain, the processing of nociceptive signals is suppressed due to resource competition.[9–11]

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Notably, working memory (WM) constitutes an essential component of executive function, optimizing attention by maintaining memory traces of attention sets and shielding goal-directed processes from interference during task execution.[11] It is essential in modulating the attention–pain interaction, primarily by balancing cognitive resources between nociceptive distraction and goal-directed attention.[12–16] The prefrontal cortex (PFC), involved in both executive functioning and pain processing, may experience competition for limited neural resources in pain distraction.[17] Effective cognitive control of pain requires diverting attention from nociceptive stimuli and maintaining task focus through WM engagement. Different WM load may directly modulate efficiency in attention regulation of pain through resource allocation mechanism.[18] Recent studies have shown that high cognitive load increases demand on attention, reducing available resources for processing extraneous stimuli and preserving task performance.[19,20] Although Deldar Z et al[20] have demonstrated that performing high load WM tasks may increase the allocation of attention resources and reduce pain perception, they also have reported that high load tasks may diminish the contribution of WM to distraction analgesia due to factors such as cognitive effort and ceiling effect, ultimately reducing the distraction analgesic effect. The competitive occupation of attention resources by cognitive fatigue can lead to increased distraction and a reduced ability to alleviate pain.[21] When WM capacity reaches the limit under high-load conditions, it results in a ceiling effect on WM-based pain inhibition.[20] These factors collectively imply a nonlinear relationship between WM load and distraction analgesia. The effect of WM load on distraction analgesia and its underlying mechanism remains further investigation.

Neurophysiological studies have shown that distraction analgesia involves decreased neural activity in pain-processing regions such as the primary somatosensory cortex (S1) and insular,[22,23] and increased activations in PFC and periaqueductal gray matter.[9] However, no studies have yet investigated functional networks of pain-related brain regions in distraction analgesia. Functional near-infrared spectroscopy (fNIRS) is a non-invasive brain imaging technique primarily used to monitor real-time changes in cortical blood oxygen metabolism to reflect neural activity. Compared to fMRI, fNIRS better accommodates comfortable posture and resists motion artifacts, enabling real-time monitoring of pain responses in this study.[24] Time-series analysis of blood-oxygen-dependent signals can capture neural activity of the brain during the process of distraction analgesia modulation. Additionally, by combining neural activity and functional connectivity between brain regions, the cortical regulatory mechanism of cognitive load dependence in distraction analgesia can be deeply understood.[25]

This study aims to verify the effectiveness of distraction analgesia at both the neural and behavioral levels, investigate the effect of n-back tasks during different WM load on pain perception and to reveal the pattern and cortical mechanism, potentially providing a neuroscientific basis for clinical cognitive-based analgesia interventions.

Material and Methods

Participants

Forty healthy participants (23 females and 17 males; 21–26 years old) were enrolled by social media platforms. Participants had a normal corrected or unaided vision and were right-handed. The exclusion criteria included (1) cardiovascular/respiratory disorders, chronic/acute pain conditions, auditory impairments, or neuropsychiatric diagnoses; (2) pregnancy status, regular drugs use, or chronic medication regimens (excluding contraceptive pills); (3) acute sleep deprivation (<6 hours before the experiment) or recent analgesic/anti-inflammatory drugs administration (<12 hours before the experiment); (4) cognitive and sensory disorders; (5) caffeine intake (<2 hours before the experiment) or intense physical activity on the day of the experiment.

Experimental Design

This experiment employed a mixed design. In the first part of the session, all participants completed a pain calibration followed by a pain-rating task (pain task). In the second part of the session, a 2 × 2 within-subject design was used to assess the distraction effect on pain perception. Participants performed an n-back WM task during two cognitive load conditions: high load (2-back) and low load (0-back), while receiving pain stimuli (with or without laser stimuli) to their right hand. All participants completed tasks in five experimental conditions: pain (laser stimuli without n-back), 0-back

(without laser stimuli), 2-back (without laser stimuli), 0-back with pain, and 2-back with pain. Pain intensity ratings and cognitive performance were recorded throughout the experiment.

Experimental Procedures

At the beginning of the study, all participants completed a brief demographic questionnaire. Then, participants underwent a pain calibration procedure. Laser stimuli were delivered to the dorsum of the right hand. After each laser stimulus, participants were instructed to verbally rate the perceived pain intensity using a Numerical Ratings Scale (NRS) ranging from 0 to 10, where 0 represented no pain and 10 represented the most unbearable pain.[26–28] Two different levels of stimuli intensity were determined for each participant, eliciting low (NRS = 4) and high (NRS = 6) pain. After pain calibration, participants were instructed to complete the pain ratings task with fNIRS recording. In the second part of the experiment, participants were required to complete both the n-back task and the n-back with pain task. They were instructed to perform the WM paradigms with fNIRS recording. The n-back task, with different WM load levels (0-back and 2-back), was used to engage WM. Before the task, participants were informed to practice the task and receive real-time feedback of their accuracy to ensure full understanding of the task. During the n-back task with pain (0-back and 2-back tasks with laser stimuli), they completed the n-back task, while pain stimuli were delivered to their dorsum of their right hand. Participants performed the n-back task and the n-back with pain task in a random order. The total duration of the experiment was approximately 50 minutes. The experimental design and procedure are shown in Figure 1.

Pain Task

Noxious laser stimuli (radiant heat) were generated using an infrared Nd:YAP laser (Electronical Engineering, Italy) with a wavelength of 1.34 μm and a pulse duration of 4 milliseconds. The He-Ne laser pulse was transmitted through optical fibers and focused by a lens to a spot approximately 7 mm in diameter,[29] synchronously activating nociceptive nerve endings in the superficial skin layers. The noxious stimuli were delivered at 2 individualized energy levels (NRS = 4 and 6) to a circular region (3 cm in diameter) on the dorsum of the right hand. A total of 30 laser stimuli (15 for each intensity) were delivered in a pseudo-randomized sequence, with an interval ranging from 20 to 21 seconds. Participants were uncertain of the exact number of pain stimuli they would experience, and the pain perception induced by laser stimuli was variable. The experiment procedure is shown in Figure 1. Each trial started with a 7–8 second fixation, followed by a short noxious stimulus delivered to the dorsum of the hand. After a 10-second interval, participants were asked to rate the perceived pain intensity using a standardized 0–10 NRS scale. To minimize the risk of nociceptor fatigue or sensitization, the laser target site was manually shifted at least 1 cm in a random direction after each stimulus.

N-Back Task

The WM task used a modified n-back paradigm, with two levels of WM load manipulation (0-back and 2-back). As a validated measure of the central executive system of WM, n-back paradigm reflects core WM functions, including attention control and updating.[30,31] It is widely utilized across psychiatric, neurological, and cognitive research domains.[32,33] The n-back paradigm was designed using E-Prime 3.0 (Psychology Software Tools, Pittsburgh, USA). Random numbers ranging from 0 to 9 were presented on the screen. In the 0-back task, participants were instructed to identify whether the current number was "0" by pressing "Q" for "yes" and "W" for "no". In the 2-back task, they were required to determine whether the current number matched the one presented before two trials, again pressing "Q" for "yes" and "W" for "no". The 0-back and 2-back task were repeated in a 0-2-0-2-0-2 sequence in three blocks, with each block containing 30 number stimuli. Thirty percent of the stimuli were target stimuli. The stimuli were presented for 1 second, and participants were given 2 seconds to respond. A 15-second rest interval was implemented between task blocks.

N-Back with Pain Task

The distraction paradigm comprised four conditions in total, each presented in two blocks: 0-back with low laser stimuli, 0-back with high laser stimuli, 2-back with low laser stimuli, and 2-back with high laser stimuli. The order was randomized. The duration of each block was fixed at 60 seconds. Before each block, a cue indicating the upcoming task (0-back or 2-back) was presented for 2 seconds. Each number in the task sequence appeared on the screen for 1000

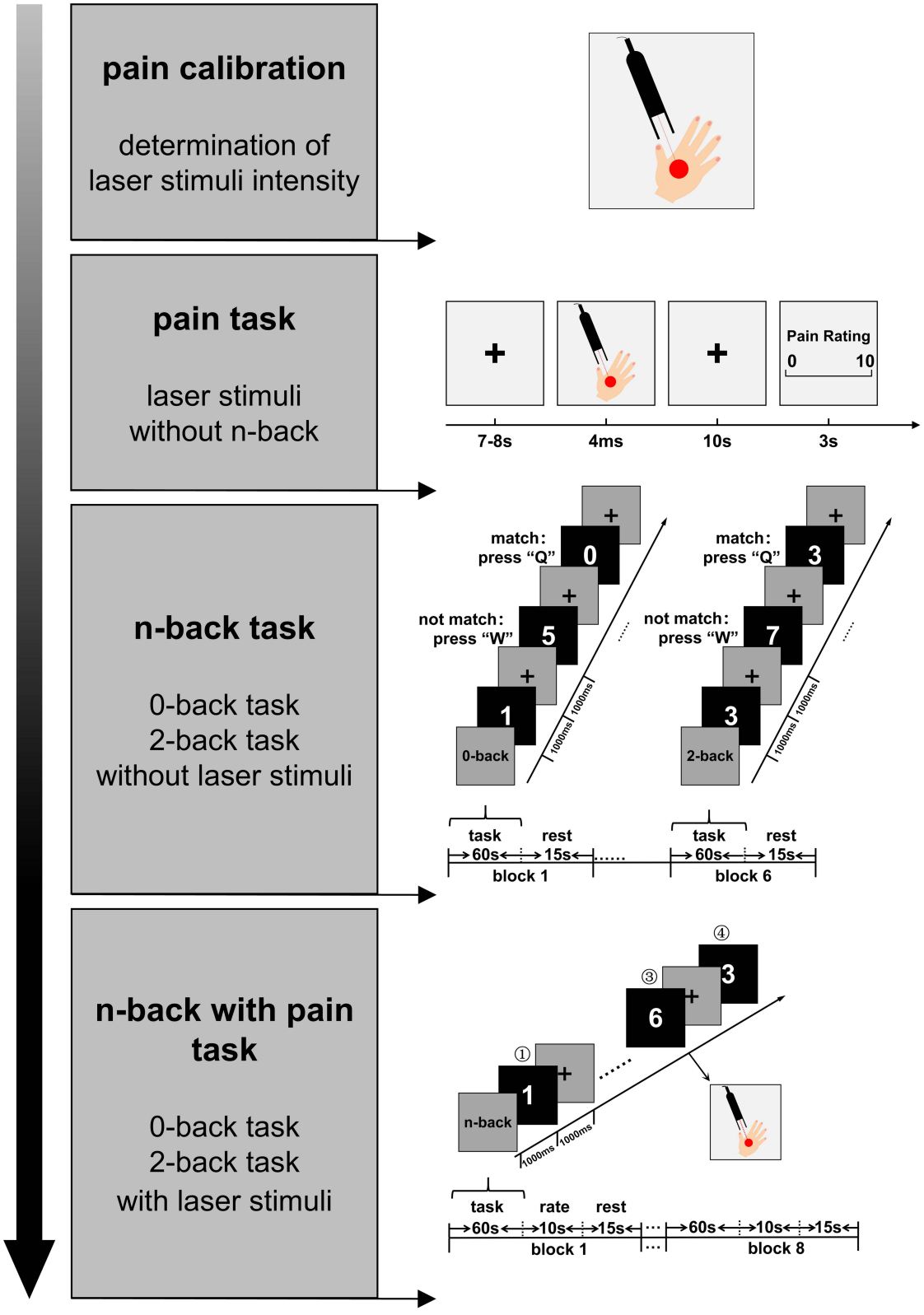

Figure 1 Experimental design and procedure.
Notes: The numbers inside the squares represent the presentation of random number stimuli. The numbers above the squares indicate the order in which the number stimuli appear (eg 1,3,4). The laser is presented once for every three number stimuli shown.

milliseconds (ms), followed by a 1000 ms blank interval. A total of 10 pain stimuli were delivered during each block. At the end of each block, a 3-second instruction was shown, instructing participants to provide a verbal rating of the perceived pain intensity using a 0–10 NRS.

fNIRS Data Acquisition

In this experiment, a fNIRS system (NirScan, Danyang Huichuang Medical Equipment Co., Ltd., Jiangsu, China) was utilized to assess cortical response from 53 channels. Three different wavelengths (730 nm, 808 nm, and 850 nm) were employed, with a sampling rate of 11 Hz to capture the near-infrared spectroscopy signals. Concentration changes in oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) were obtained based on the modified Beer-Lambert law. The optical system consisted of 18 sources and 18 detectors, with adjacent sources and detectors spaced 3 cm apart. The connection between sources and detectors was defined as a channel. The coordinates of each probe were determined based on the International 10–20 system and the coordinate localization feature of SPM software, referencing both the coordinates and the optical electrode positions on the Montreal Neurological Institute (MNI) brain template. Figure 2A shows the complete arrangement of the fNIRS probes and channels, while Figure 2B shows the location of the 41 selected channels out of 53, covering 9 brain regions of interest: right and left secondary somatosensory cortex (RS2; LS2), right and left premotor cortex (RPMC; LPMC), right and left primary somatosensory cortex (RSM1; LSM1), right and left dorsolateral prefrontal cortex (RDLPFC; LDLPFC), and anterior prefrontal cortex (aPFC).

fNIRS Preprocessing and Analysis

In this study, fNIRS signals were preprocessed and analyzed using NirSpark software (HuiChuang, China) and matlab (Mathworks, MA, USA). First, we conducted a preliminary inspection of the raw data, identifying and removing channels with poor signal quality. Signal quality was assessed based on the coefficient of variation (cv), where values ≤5 were considered good, 5–20 were considered acceptable, and >20 were considered poor. Next, the raw light intensity data series were converted into optical density (OD) changes. We applied spline interpolation to correct motion artifacts in the channels. Motion artifacts typically manifest as pulsatile or abrupt jumps caused by relative movement between the

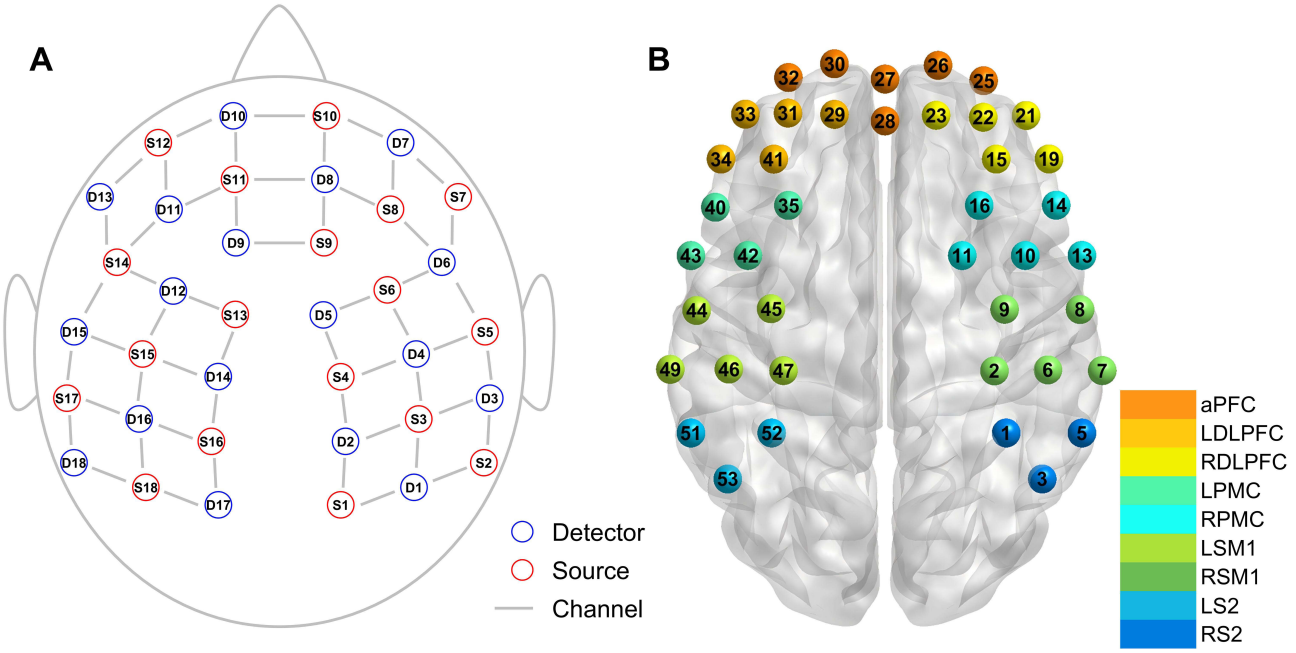

Figure 2 fNIRS channel settings.
Notes: fNIRS 36-probe and 53-channel montage placement (**A**) and the distribution of fNIRS 53-channel in S2, PMC, SM1, DLPFC and aPFC (**B**). The numbers in (**A**) represent 18 light sources and detectors. The numbers in (**B**) represent 53 channels.
Abbreviations: aPFC, anterior prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; PMC, premotor cortex; SM1, primary somatosensory cortex; S2, secondary somatosensory cortex; L, left; R, right; S, source; D, detector.

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scalp and the probe.[34] We applied a bandpass filter (0.01–0.2 Hz) to remove physiological noise, such as respiration, cardiac activity, and low-frequency signal drift. Subsequently, based on the modified Beer-Lambert law, we calculated changes in oxygenated hemoglobin (HbO), deoxygenated hemoglobin (HbR), and total hemoglobin (HbT) concentrations.

During the analysis phase, we focused on data from 41 channels that covered nine ROIs, which are significantly associated with pain based on previous studies. Specifically, multiple studies have demonstrated that brain regions such as S1, S2, M1, aPFC, DLPFC and PMC are critical for pain processing.[35] Previous studies on distraction analgesia have confirmed that during the process of distraction, activation in brain regions such as the insula and S1 decreases, while neural responses in regions including the DLPFC and parietal lobe show increased activation and reduced functional connectivity.[36] Meanwhile, brain function studies related to analgesia have also reported that when pain perception decreases, the activation level of SM1 and its functional connectivity with the DLPFC/S1 are significantly reduced.[37] Different time windows were set to extract stable hemoglobin time series: for the pain task, the time window was 13 seconds after each stimulus; for the n-back task, the time window was 30 seconds; and for the n-back with pain task, the time window was 60 seconds. The 2-second pre-task period was used as a baseline for correction. By averaging across all blocks for each task, we generated the mean hemodynamic reaction time series curves related to the task. Previous studies have shown that HbO is more sensitive to changes in brain region blood flow signals than HbR,[38,39] therefore, we primarily focused on the changes in the mean HbO values under different task conditions as indicators of brain activation.

To further explore the load-dependent neural mechanism of distraction analgesia, we conducted functional connectivity analysis to observe the inter-regional connectivity of the brain during different tasks. The relative changes in HbO concentration within each block were extracted for functional connectivity analysis using the brain network module in the NirSpark software package. Pearson correlation coefficients between the HbO concentrations of different brain regions in the time series were calculated, followed by Fisher Z transformation. The transformed values were then defined as the functional connectivity strength.

Statistical Analysis

Data was analyzed using IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp). The measured data were expressed as means and standard deviations. Normality of the data was assessed using the Shapiro–Wilk test. Independent samples t-tests and paired t-tests were applied for normally distributed continuous variables, while non-parametric tests were used for variables that were not normally distributed. To compare the effect of different WM loads on pain ratings, a one-way repeated measures analysis of variance (ANOVA) was conducted, with false discovery rate (FDR) correction applied. At the neural level, we first verified whether pain elicited activation in the corresponding brain regions by conducting paired t-tests on the HbO mean values for the n-back task and n-back with pain task, with FDR correction applied. Secondly, we analyzed the impact of WM load on pain-related neural activity by conducting paired t-tests on the HbO mean values for 0-back with pain task and 2-back with pain task, with FDR correction applied. To examine whether WM load influenced pain-related behavior through alterations in pain-related neural activity, a mediation analysis was conducted by using the SPSS 25 (test of joint significance approach) and Mplus8.11 (path-analytic method).[40] In this model, the independent variable (X) represented the WM load (0-back = 1; 2-back = −1), the dependent variable (Y) was the pain-related behavioral measures (defined as the change in pain ratings on the NRS), and the mediator (M) was the pain-related neural activity. Pain-related neural activity and behavioral measures were measured twice in the same subject at both WM loads. The pain-related behavioral or neural measures were quantified as the contrast between the n-back with pain task and n-back task. They were measured twice in the same subject at both WM loads. The indirect effect was considered statistically significant when the 95% confidence interval (CI) did not include zero, with a significance threshold set at $p < 0.05$. Additionally, a two-way repeated measures ANOVA was used to compare the differences in functional connectivity between brain regions across the n-back and n-back with pain tasks, and simple effects analysis was conducted when the interaction effect was significant. To assess the interference of pain on cognitive task performance, a two-way repeated measures ANOVA was conducted to compare WM reaction time (RT) and accuracy (ACC) for each task (0-back and 2-back) when performed with or without pain. Simple effects analysis was

conducted when the interaction effect was significant, with FDR applied. The partial eta squared (η^2p) effect sizes of significant effects in the ANOVA were reported, where 0.01 represented a small effect, 0.06 represented a medium effect, and 0.14 represented a large effect.[41] Statistical significance was set at $p < 0.05$ for all tests, and all p - values were two-tailed.

Power Analysis

The primary outcome of this study was the effect of WM load on pain ratings, which was assessed using a one-way repeated measures ANOVA. An a priori power analysis conducted with G*Power 3.1, assuming a medium effect size (f = 0.25), a significance level of $\alpha = 0.05$, and a statistical power of $(1 - \beta) = 0.80$, indicated a required sample size (n = 28), ensuring adequate power at the behavioral level. To ensure sufficient power for neural and connectivity analyses, additional power calculations were performed for paired-sample t-tests and two-way repeated measures ANOVA. The sample size are n = 27 and n = 24. The largest sample size among these analyses was adopted as the reference (n = 28). Considering a 10–15% attrition rate, a minimum of 32 participants should be enrolled in the study. Thus, the study was sufficiently powered across behavioral, neural, and connectivity measures.

Results

Descriptive Statistics

Five participants were excluded from the initial sample of N = 40. Data from 2 participants were incomplete due to missing marking records caused by equipment failure. In addition, data from 3 participants were excluded due to excessive motion during the task phase of fNIRS measurements (n = 2) and poor signal quality in some channels caused by inadequate fitting of the measurement cap to the head shape (n = 1). Thus, we analyzed data from 35 participants. Table 1 presents the baseline demographic and pain-related clinical characteristics of the participants. The gender ratio of participants included in this study was not balanced. Results from baseline-related questionnaires have excluded the confounding effect of gender, confirming the homogeneity and stability of the study sample.

Modulation of Pain Ratings by WM Load

As shown in Figure 3, Repeated measures ANOVA was performed on the perceived pain intensity NRS ratings during different conditions (pain, 0-back with pain, and 2-back with pain). The results showed significant differences in pain intensity ratings across conditions ($F = 17.666$; $p < 0.001$***; $\eta^2p = 0.342$). Compared to the pain task, NRS were significantly lower in both 0-back with pain ($p = 0.001$**) and 2-back with pain ($p < 0.001$***). Additionally, NRS was significantly lower in the 2-back with pain compared to 0-back with pain ($p = 0.002$**).

Table 1 Demographic and Pain-Related Clinical Characteristics of the Participants

	Male (n = 13)	Female (n = 22)	Statistics
Age (y)[a]	23.462 ± 2.145	23.500 ± 1.439	$t = -0.06$, $p = 0.95$
PSQ[a]	65.846 ± 17.339	61.591 ± 18.144	$t = 0.68$, $p = 0.50$
FPQ[a]	60.462 ± 8.383	58.636 ± 18.531	$t = 0.40$, $p = 0.69$
PASS[a]	45.769 ± 10.167	41.455 ± 16.124	$t = 0.87$, $p = 0.39$
PVAQ[a]	39.077 ± 7.065	37.455 ± 6.053	$t = 0.72$, $p = 0.48$
PCS[a]	22.846 ± 8.735	22.136 ± 9.853	$t = 0.21$, $p = 0.83$
SDS[a]	32.385 ± 4.874	35.682 ± 6.636	$t = -1.56$, $p = 0.13$
Low Stimulus Intensity (J)[a]	3.019 ± 0.360	2.966 ± 0.356	$t = 0.43$, $p = 0.67$
High Stimulus Intensity(J)[a]	3.558 ± 0.273	3.409 ± 0.412	$t = 1.16$, $p = 0.26$

Notes: Data are expressed using Mean ± SD. Statistics were obtained by comparing males and females to exclude gender effects. [a]means Independent-sample *t* test.

Abbreviations: PSQ, pain sensitivity questionnaire; FPQ, fear of pain questionnaire; PASS, pain anxiety symptom scale; PVAQ, pain vigilance and awareness questionnaire; PCS, pain catastrophizing scale; SDS, Self-Rating Depression Scale.

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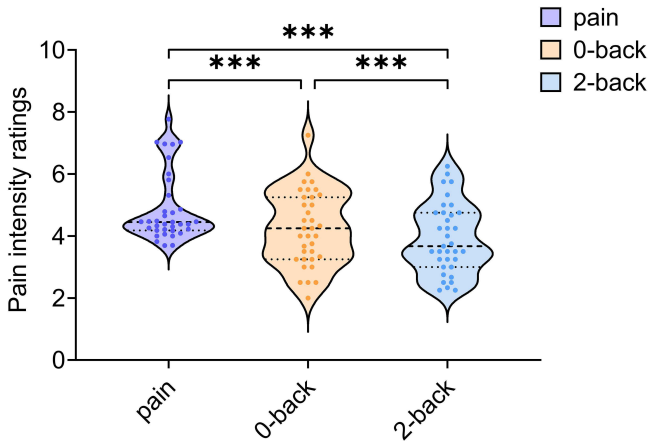

Figure 3 Pain ratings in pain task and n-back with pain task.
Notes: Violin plots show the data distributions, mean (dashed line), and quartiles (black line). Each colored dot represents an individual participant. ***$p < 0.001$.

Modulation of Pain-Related Brain Activity by WM Load

In the whole-brain analysis, noxious laser stimuli activated a broad range of brain areas associated with pain, including RS2 ($t = 2.473$, $p = 0.034$*), RPMC ($t = 3.108$, $p = 0.012$*), RSM1 ($t = 2.210$, $p = 0.044$*), LSM1 ($t = 2.262$, $p = 0.044$*), RDLPFC ($t = 3.932$, $p < 0.001$***), LDLPFC ($t = 2.716$, $p = 0.023$*), and aPFC ($t = 3.655$, $p = 0.005$**), as shown in Table 2 and Figure 4.

Further comparison of brain activation during 0-back with pain and 2-back with pain task revealed significant decreases in activation in the left S2 ($t = 2.757$, $p = 0.041$*) and left SM1 ($t = 2.834$, $p = 0.041$*) regions during 2-back with pain, as shown in Table 3 and Figure 5. Mediation analysis was used to determine the contribution of neural activity in the effect of cognitive load on pain perception. As shown in Figure 6, WM load indirectly affected pain intensity by modulating brain activity in the LSM1 (a*b = −0.014, SE = 0.039, CI = [−0.102, 0.059]) and in the LS2 (a*b = 0.004, SE = 0.050, CI = [−0.112, 0.096]), but the effects were not significant. The point estimates of the indirect effects were not close to zero. The result is more likely attributed to insufficient statistical power (limited sample size) rather than a genuine absence of the mediating effect. Thus, the results could not confirm the mediating role of LSM1/LS2 neural activity, but they also do not rule out this potential pathway. A two-way repeated measures ANOVA was used to compare the functional connectivity between brain regions during different tasks. Significant interaction effects were found in the functional connectivity between RS2-aPFC ($F = 6.475$, $p =$

Table 2 Effect of N-Back with Pain Task on Brain Responses to Pain Stimuli

ROI	Mean	SD	LCI (95%)		t	p
RS2	0.021	0.050	0.004	0.038	2.473	0.034*
LS2	0.020	0.056	0.0003	0.039	2.061	0.053
RPMC	0.021	0.040	0.007	0.035	3.108	0.012*
LPMC	0.005	0.047	−0.011	0.021	0.643	0.524
RSM1	0.020	0.054	0.002	0.039	2.210	0.044*
LSM1	0.024	0.062	0.002	0.045	2.262	0.044*
RDLPFC	0.024	0.037	0.012	0.037	3.932	<0.001***
LDLPFC	0.015	0.032	0.004	0.026	2.716	0.023*
aPFC	0.025	0.040	0.011	0.039	3.655	0.005**

Notes: Pain activation in the corresponding brain regions by conducting paired t-tests on the HbO mean values for the n-back task and n-back with pain task, with FDR correction applied. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
Abbreviations: aPFC, anterior prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; PMC, premotor cortex; SM1, primary somatosensory cortex; S2, secondary somatosensory cortex.

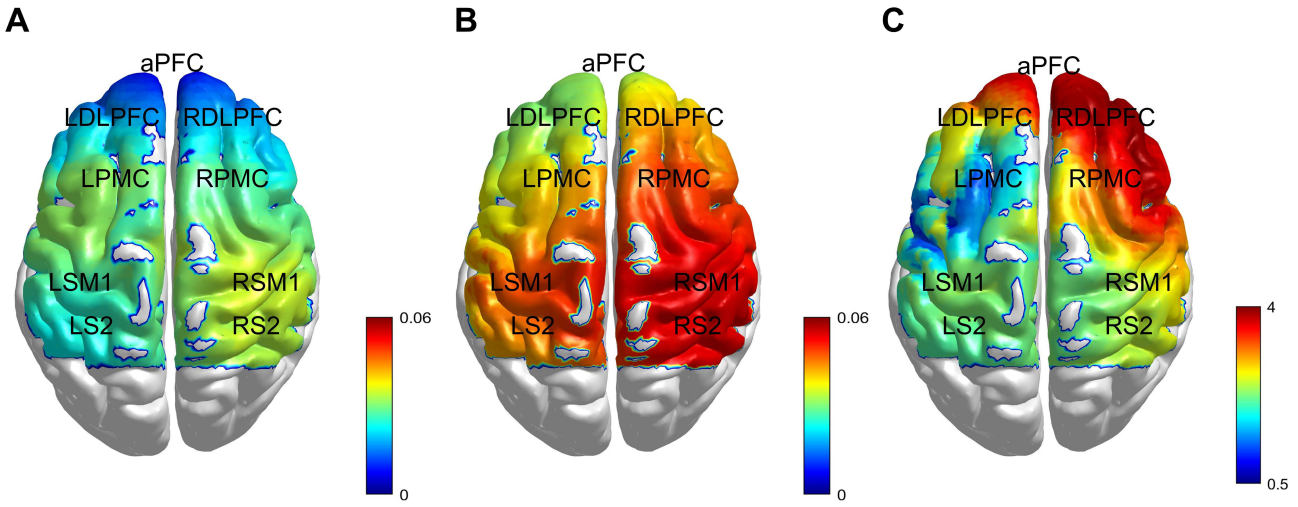

Figure 4 Brain activation during the n-back and n-back with pain task.
Notes: Brain activation plots for n-back (**A**), n-back with pain (**B**) and the difference (**C**). The redder the color in the brain map, the greater the activation.
Abbreviations: aPFC, anterior prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; PMC, premotor cortex; SM1, primary somatosensory cortex; S2, secondary somatosensory cortex; L, left; R, right.

0.016*, $\eta^2p = 0.160$), RSM1-RDLPFC ($F = 6.225$, $p = 0.018$*, $\eta^2p = 0.155$), RSM1-aPFC ($F = 7.439$, $p = 0.010$**, $\eta^2p = 0.180$), and LSM1-aPFC ($F = 6.523$, $p = 0.015$*, $\eta^2p = 0.161$), as shown in Table 4. Simple effects analysis was conducted on the significant interaction effects in the functional connectivity between brain regions.

The results revealed that during high load task, the additional pain stimuli in the n-back with pain task reduced the functional connectivity between brain regions compared to the n-back task in RS2-aPFC ($p = 0.003$**), RSM1-RDLPFC ($p < 0.001$***), RSM1-aPFC ($p = 0.004$**), and LSM1-aPFC ($p = 0.034$*), as shown in Figure 7A. Functional connectivity in the n-back task increased in RS2-aPFC ($p = 0.002$**), RSM1-RDLPFC ($p = 0.002$**), and RSM1-aPFC ($p = 0.003$**) with increasing load, as shown in Figure 7B.

Interference of Pain with Cognitive Performance

A two-way repeated measures ANOVA was conducted to compare WM RT and ACC for each task (0-back and 2-back) when performed with or without pain. No significant interaction effects were found between WM load and pain intensity

Table 3 Brain Responses to N-Back with Pain Task with Different WM Load

ROI	Mean	SD	LCI (95%)		t	p
RS2	0.025	0.065	0.003	0.048	2.302	0.063
LS2	0.029	0.062	0.008	0.050	2.757	0.041*
RPMC	0.022	0.064	−0.0002	0.044	2.007	0.068
LPMC	0.022	0.067	−0.001	0.045	1.940	0.069
RSM1	0.019	0.056	0.0003	0.039	2.066	0.068
LSM1	0.032	0.067	0.009	0.055	2.834	0.041*
RDLPFC	0.016	0.051	−0.002	0.033	1.814	0.078
LDLPFC	0.017	0.048	0.0002	0.033	2.058	0.068
BA10	0.022	0.055	0.003	0.041	2.392	0.063

Notes: The effect of WM load on pain-related neural activity by conducting paired t-tests on the HbO mean values for 0-back with pain task and 2-back with pain task, with FDR correction applied. *$p < 0.05$.
Abbreviations: aPFC, anterior prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; PMC, premotor cortex; SM1, primary somatosensory cortex; S2, secondary somatosensory cortex.

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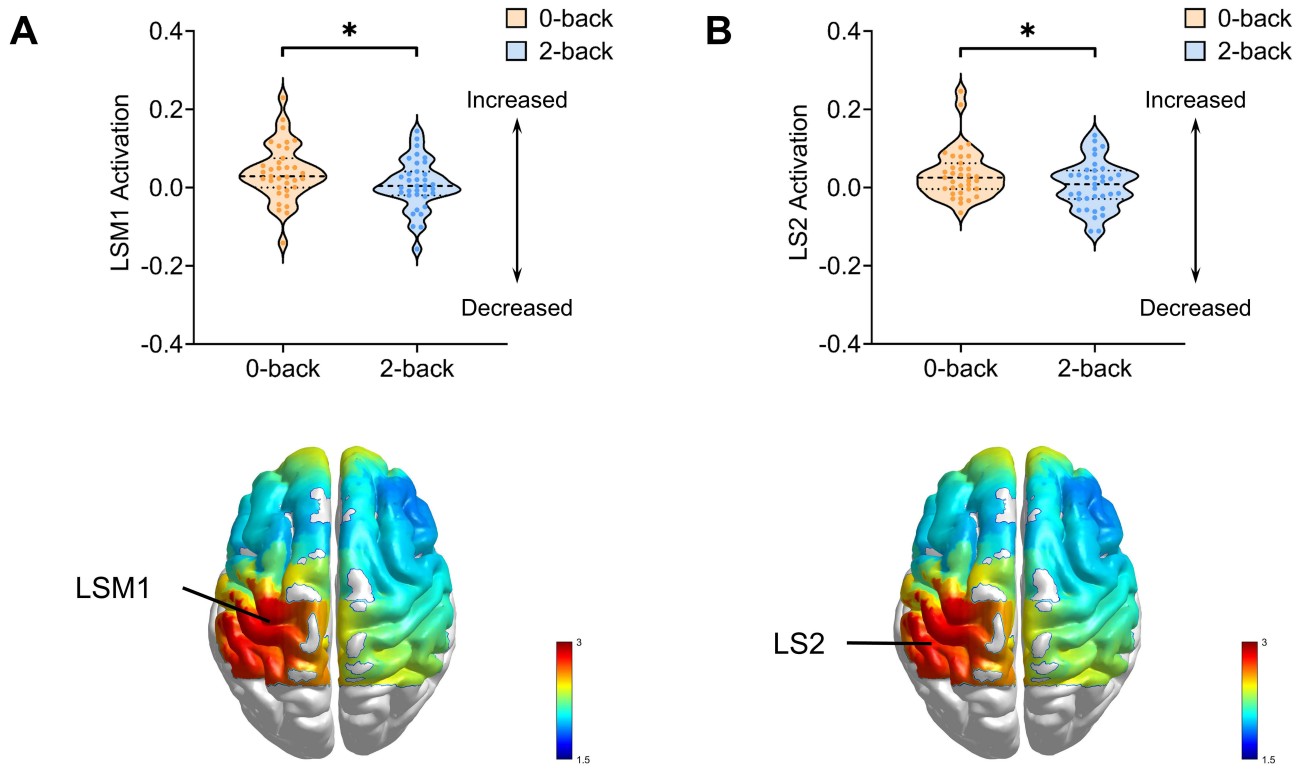

Figure 5 Brain activation differences during the n-back with pain task during different WM load in LS2 and LSM1.
Notes: Violin plots and brain activation plots for LS2 (**A**) and the LSM1 (**B**). Violin plots show the data distributions, mean (dashed line), and quartiles (black line). Each colored dot represents an individual participant. Positive values represent positive activation (increase), negative values represent negative activation (decrease). The redder the color in the brain map, the greater the activation. *$p < 0.05$.
Abbreviations: LSM1, left primary somatosensory cortex; LS2, left secondary somatosensory cortex.

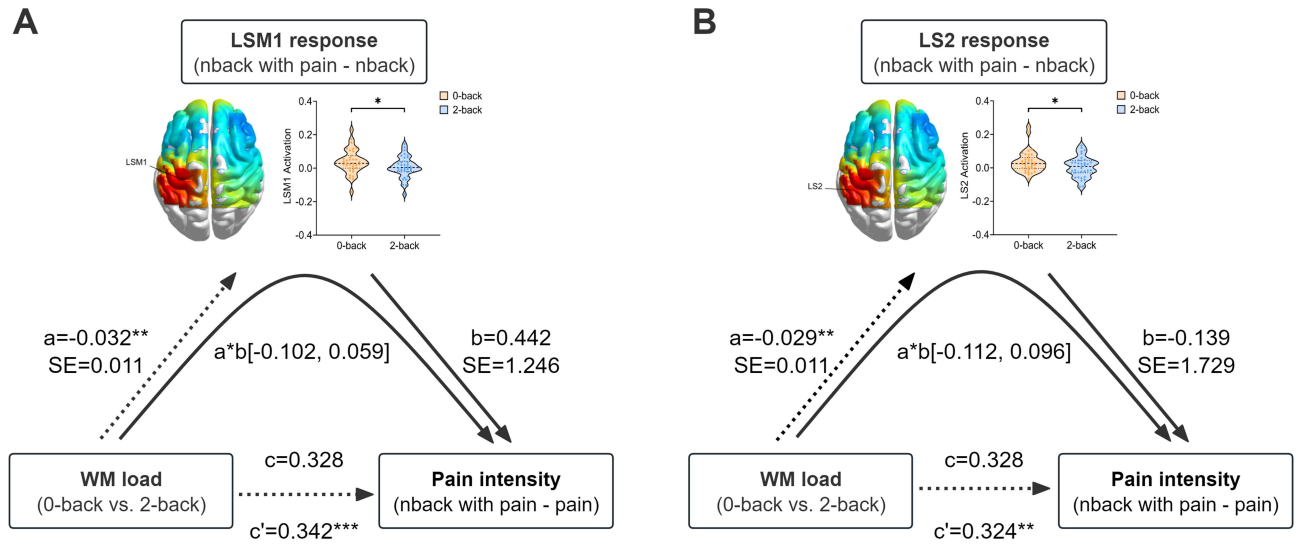

Figure 6 Mediating role of neural responses on the effect that WM had on pain perception.
Notes: Mediating role of LSM1 neural responses (**A**) and LS2 neural responses (**B**) on the effect that WM had on pain perception. Violin plots show the data distributions, mean (dashed line), and quartiles (black line). Each colored dot represents an individual participant. The redder the color in the brain map, the greater the activation. Dotted paths indicate significance, while solid paths indicate non-significance. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
Abbreviations: LSM1, left primary somatosensory cortex; LS2, left secondary somatosensory cortex. SE, standard error.

Table 4 Effect of WM Load and Pain Distraction on Brain Functional Connectivity

ROI	Interaction Effect			WM load Effect	Pain Distraction Effect
	F	*p*	η^2_p	*p*	*p*
RS2 - aPFC	6.475	0.016*	0.160	0.022*	0.012*
RSM1 - RDLPFC	6.225	0.018*	0.155	0.010*	0.0004***
RSM1 - aPFC	7.439	0.010*	0.180	0.023*	0.033*
LSM1 - aPFC	6.523	0.015*	0.161	0.512	0.341

Notes: A two-way repeated measures ANOVA was used to compare the differences in functional connectivity between brain regions across the n-back and n-back with pain tasks. The effect of WM load effect (0-back and 2-back), Pain distraction effect (with or without pain), and the Interaction effect was shown in this table *$p < 0.05$; ***$p < 0.001$.

Abbreviations: aPFC, anterior prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; SM1, primary somatosensory cortex; S2, secondary somatosensory cortex.

on ACC ($F = 0.628$, $p = 0.434$) and RT ($F = 0.0005$, $p = 0.983$). Focusing on the main effects, significant main effects of WM load were found on both ACC ($F = 28.799$, $p < 0.001$***, $\eta^2p = 0.459$) and RT ($F = 61.253$, $p < 0.001$***, $\eta^2p = 0.643$). Additionally, a significant main effect of pain was found in ACC ($F = 5.346$, $p = 0.027$*, $\eta^2p = 0.136$), as shown in Figure 8.

Discussion

This study used fNIRS to explore cognitive load-dependent perception modulation and cortical mechanism in distraction analgesia in healthy individuals. The results showed that high-load WM significantly reduced the perceived intensity[42] and pain-related neural activation in the S2 and SM1. Under high load, the functional connectivity between brain regions

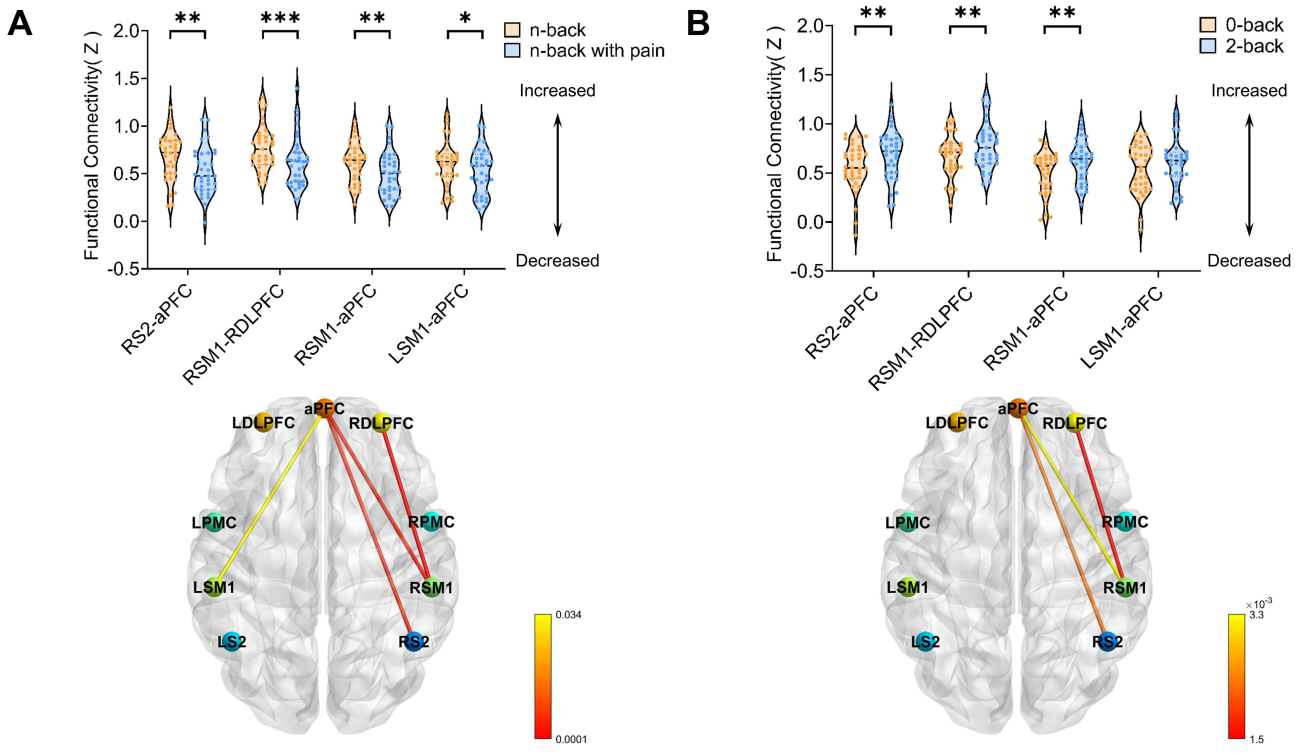

Figure 7 Results of functional connectivity differences within the high load WM and the n-back.

Notes: Violin plots and FC plots for the high load WM (**A**) and the n-back (**B**). Violin plots show the data distributions, mean (dashed line), and quartiles (black line). Each colored dot represents an individual participant. The redder the color in the line of the brain map, the greater the differences. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

Abbreviations: aPFC, anterior prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; SM1, primary somatosensory cortex; S2, secondary somatosensory cortex; L, left; R, right.

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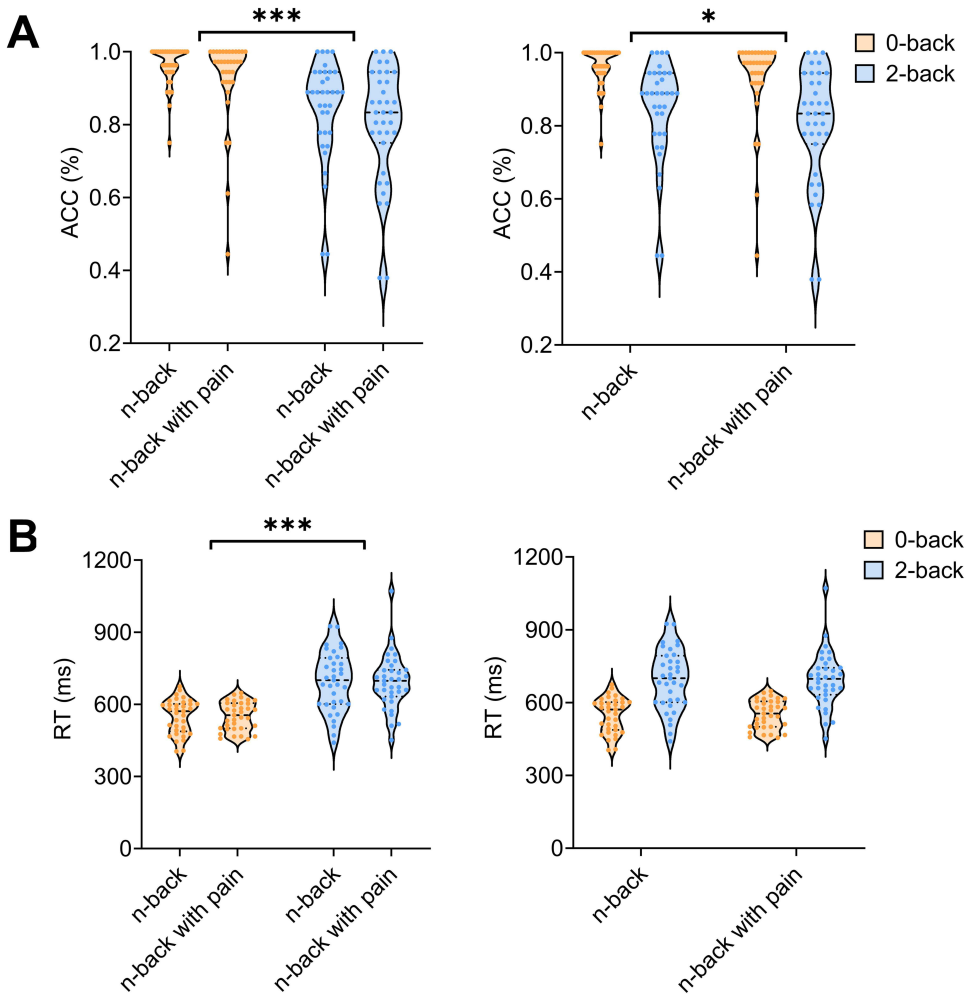

Figure 8 Reaction time and accuracy during different WM load.
Notes: Reaction time during different WM load (**A**) and accuracy during different WM load (**B**). Violin plots show the data distributions, mean (dashed line), and quartiles (black line). Each colored dot represents an individual participant. *$p < 0.05$; ***$p < 0.001$.
Abbreviations: ACC, accuracy; RT, reaction time.

(RS2-aPFC, RSM1-RDLPFC, RSM1-aPFC, and LSM1-aPFC) was significantly lower during the n-back with pain task compared to the n-back task. It indicated that as WM load increased, the coupling between the network involved in pain processing was significantly attenuated.

Based on the neurocognitive model of pain, WM regulates the allocation of attention resources through central executive system, and its load levels directly affect the effectiveness of pain perception suppression.[43] This study systematically revealed the gradient effect of WM load on pain perception inhibition by manipulating load levels of WM. We found that WM significantly reduced pain ratings, with the analgesic effect of the 2-back task being greater than that of the 0-back task. Our findings were consistent with prior research,[20] which involves shifting cognitive resources away from pain and prioritizing task-related stimuli through "top-down" control. This reduces the occupation of limited cognitive resources by pain, thereby decreasing pain perception.[7] Furthermore, considering that pain expectation and continuous stimulation may lead to a decline in perceptual levels,[44] we set two different pain levels and randomized both the spatiotemporal delivery (arrival and location) and intensity levels of noxious stimuli. This setting effectively avoided interference from expectation effects and sensory habituation during pain assessment,[45] reinforcing the central role of the resource competition theory. Although this study found a positive correlation between WM load and pain suppression, previous research suggests that this modulation pattern may be influenced by factors such as cognitive fatigue and ceiling effects.[20] A pain study by Zoha Deldar et al[20] found that both 0-back and n-back tasks reduced pain, with n-back being

more effective than 0-back, but no significant differences in pain suppression were observed between 2-back and 3-back tasks. Based on the research by Vogel et al[21], we proposed potential explanations for the absent analgesic effect in n-back tasks. WM affects the allocation of attention resources in competition, when load exceeds individuals' execution capacity threshold, indirectly reversing the analgesic advantage and reducing the contribution of WM to distraction analgesia. Therefore, the ceiling effect caused by limited WM capacity is one of the important factors affecting distraction analgesia. Future research can establish a multi-gradient model of WM capacity and assess individual difference in execution function to explore the optimal load range for maximizing analgesic effects.

At the neural level, analgesia effects induced by WM distraction might involve a hierarchical gate control mechanism driven by PFC. We compared brain activation between the n-back task and the n-back with pain task, and found that SM1, S2, PMC, aPFC, and DLPFC were activated during pain stimuli in the n-back with pain task, forming a dynamic regulatory network for pain processing.[35] SM1 and S2 are involved in nociceptive pain and sensory processing,[46,47] and more significant brain activation during 0-back suggests less inhibitory effect of low WM load on pain processing. As WM load increased, activation in the S2 and SM1 decreased during the n-back with pain task. We supposed that high WM load might enhance thalamocortical inhibitory gating, resulting in suppression of nociceptive signal transmission from S2 and SM1. An fMRI study by Valet et al[48] showed that attention diversion induced by single cognitive load Stroop tasks reduced brain activities encoding pain, such as the thalamus and somatosensory cortex, supporting the effect of distraction analgesia at a single-load level. Moreover, an fMRI study by Legrain V et al[49,50] found that when focusing on a primary visual task, the responses in S1/M1 and the insula to noxious stimuli are reduced. Neural responses in S1/S2 are affected by attention loads, with the spatial pattern of distraction analgesia being highly consistent with the findings of this study. Based on fNIRS data, this study further suggests that WM distraction modulates pain processing through "top-down" attention regulation, reducing somatosensory cortical neural activity and thus affecting the processing of pain stimuli.

We conducted mediation analysis on the neural responses of the SM1 and S2 regions to test whether WM loads indirectly affected pain ratings through brain activation. The results showed no significant mediation effect, indicating that the effect of loads on pain ratings was not completely dependent on the neural response changes in individual brain regions. The effect of distraction analgesia may involve a complex functional network. Therefore, to observe the changes in brain functional networks induced by distraction under different loads, we calculated the functional connectivity between target brain regions.

The results of the functional connectivity between target brain regions indicated that with increasing load, functional connectivity in the WM task increased between RS2-aPFC, RSM1-aPFC, and RDLPFC-RSM1, reflecting the recruitment of "top-down" modulatory resources at the cortical level due to WM load. However, as the load increased, the additional pain stimuli in the n-back with pain task reduced the functional connectivity between the RS2-aPFC, bilateral SM1-aPFC, and RDLPFC-RSM1 brain regions compared to the n-back task. The results indicated that high load distraction inhibited the control of the sensory cortex by the PFC and reduced the coupling between pain-related brain networks, which might be related to the saturation effect in prefrontal control pathways. The DLPFC supports executive control over attention, WM, and pain inhibition via top-down modulation.[51,52] aPFC, an essential component of the PFC, contributes to self-referential processing, attention regulation, WM, decision-making, and salience detection. These findings indicated that aPFC was important in appropriate attention shift and the reallocation of pain awareness and response.[35] The functional connectivity between the PFC and SM1 might indicate the contribution of prefrontal cognitive processing to pain processing. The PFC might be a key node in the network related to nociceptive processing and pain regulation, transmitting core pain processing through its connection with SM1.[52] A study by Peng Weiwei et al[37] found that α-tACS on SM1 may inhibit pain perception and neural responses by decoupling SM1 from key sensory-motor, emotional, and cognitive processing networks involved in pain. Similar findings were also reported by Wagner et al in their study on placebo analgesia.[53] They found that placebo manipulation may exert analgesic effects by decoupling the somatosensory network responsible for pain processing from the descending modulatory network. Furthermore, Deng xue et al[54,55] reported that VR-induced analgesia, as shown in fNIRS studies, is characterized by reduced S1 connectivity and diminished pain-related processing. The weakened coupling between cortical pain-related regions and other brain areas may serve as a critical mechanism disrupting normal pain signaling, consistent with our findings. Therefore, we

speculated that WM distraction analgesia may similarly reduce pain through decoupling the core networks involved in pain perception and cognitive processing.

We also examined the potential impact of pain on WM performance. A significant main effect of pain intensity on ACC was observed, indicating that the presence of pain significantly impaired WM performance. This damage might arise through two potential pathways. Pain signals are transmitted through the spinal-thalamic-cortical pathway to cortical regions such as S1 and S2.[56] Through inter-regional neural connectivity or reorganization, the PFC evaluates pain and allocates attention, thereby competing for cognitive resources and reducing the neural encoding precision of WM representations.[57] Additionally, the insula and DLPFC, as key regions for cognitive control, may be involved in analgesia processing. This mechanism might relate to diminished "top-down" cognitive control from the DLPFC to the insula, ACC, and thalamus.[58–61] Pain-induced negative emotions may decrease the coupling of the PFC and ACC during cognitive reappraisal.[22] Moreover, there was no significant interaction between WM load and pain in terms of accuracy, suggesting that the impairing effect of pain might be similar under both 0-back and 2-back conditions. In high-load condition, the increase in reaction time alongside a decrease in accuracy supports Baddeley's limited capacity theory of the central executive system.[62] When cognitive demand exceeds the individual's resource threshold, the cost of conflict monitoring in the ventral attention network (VAN) increases, and more time is needed for information matching and conflict resolution.[63] Notably, the observed "speed-accuracy decoupling" under pain conditions suggests the adoption of a behavioral compensation strategy, whereby participants maintain response speed at the expense of accuracy.[64] Our findings support the hierarchical hypothesis of the attention competition model, demonstrating that pain disrupts cognition through two mechanisms: (1) direct competition for prefrontal resources, and (2) emotion-mediated impairment of cognitive control networks.[22] This provides a new interpretation for cognitive deficits observed in chronic pain. Prolonged pain may reconstruct neural networks, reduce the availability of cognitive resources and reinforce negative affective processing in the limbic system,[65,66] leading to a vicious "pain-cognition" cycle and driving the brain's functional reorganization toward a "pain salience-prioritized" mode. Future research may focus on interventions such as neurofeedback training, transcranial electrical stimulation, or virtual reality-based distraction tasks to reconstruct neural connectivity, and improve cognitive impairments in chronic pain patients.

The results of the current study should be considered within the study design and its potential limitations. First, as the participants were all young and healthy university students, the findings may not be generalizable to broader or more diverse populations. Second, the load of the WM paradigm was simple. Future research could use more refined gradients and incorporate broader attention tests. Third, the indirect effects of WM load on pain ratings via LSM1/LS2 did not reach significance, which may be attributed to insufficient statistical power. Future research could expand the sample size and improve measurement precision.

Conclusion

Our study demonstrates that WM distraction reduces both pain perception and neural responses to experimental laser pain stimuli in healthy individuals and that a significant reduction in functional coupling between regional networks involved in pain processing was observed. Therefore, our findings suggest that WM load may reduce pain perception by decreasing neural responses in pain-related regions and promoting the decoupling of related brain networks, providing neuroscientific evidence for cognitive strategy-based analgesia interventions.

Data Sharing Statement

For additional details, please reach out to the corresponding author. The datasets analyzed in this study can be obtained from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

All participants gave written informed consent. The study procedures were approved by the Ethics Committee of Zhujiang Hospital, Southern Medical University (Ethical approval number: 2024-KY-427-02). The clinical registration number is ChiCTR2500100508. This study complies with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author(s) report no conflicts of interest in this work.

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