PAIN® 154 (2013) 2060–2071

PAIN®

www.elsevier.com/locate/pain

Neural underpinnings of behavioural strategies that prioritize either cognitive task performance or pain

Nathalie Erpelding [a], Karen D. Davis [a,b,c,*]

[a] Division of Brain, Imaging, and Behaviour—Systems Neuroscience, Toronto Western Research Institute, University Health Network, Toronto, Ontario, Canada
[b] Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada
[c] Department of Surgery, University of Toronto, Toronto, Ontario, Canada

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ARTICLE INFO

Article history:
Received 24 April 2013
Received in revised form 3 June 2013
Accepted 17 June 2013

Keywords:
Attention
Cognitive interference
CTA
fMRI
Pain
Resting-state connectivity
sMRI
TBSS
VBM

ABSTRACT

We previously discovered that when faced with a challenging cognitive task in the context of pain, some people prioritize task performance, while in others, pain results in poorer performance. These behaviours, designated respectively as A- and P-types (for attention dominates vs pain dominates), may reflect pain coping strategies, resilience or vulnerabilities to develop chronic pain, or predict the efficacy of treatments such as cognitive behavioural therapy. Here, we used a cognitive interference task and pain stimulation in 80 subjects to interrogate psychophysical, psychological, brain structure and function that distinguish these behavioural strategies. During concurrent pain, the A group exhibited faster task reaction times (RTs) compared to nonpain trials, whereas the P group had slower RTs during pain compared to nonpain trials, with the A group being 143 ms faster than the P group. Brain imaging revealed structural and functional brain features that characterized these behavioural strategies. Compared to the performance-oriented A group, the P group had (1) more gray matter in regions implicated in pain and salience (anterior insula, anterior midcingulate cortex, supplementary motor area, orbitofrontal cortex, thalamus, caudate), (2) greater functional connectivity in sensorimotor and salience resting-state networks, (3) less white matter integrity in the internal and external capsule, anterior thalamic radiation and corticospinal tract, but (4) were indistinguishable based on sex, pain sensitivity, neuroticism, and pain catastrophizing. These data may represent neural underpinnings of how task performance vs pain is prioritized and provide a framework for developing personalized pain therapy approaches that are based on behaviour–structure–function organization.

1. Introduction

Intuitively, pain should interfere with the ability to sustain a high level of performance during an attention-demanding task. However, we discovered that some individuals improve cognitive task performance in the context of pain (ie, attention dominates, designated A-type), whereas others show decline of cognitive task performance during pain (ie, pain dominates, designated P-type) [76]. These behavioural strategies may lie at the core of understanding individual variability in pain coping strategies and the effectiveness of multidimensional treatment approaches for pain such as cognitive behavioural therapy.

It is not known why in some individuals (P-type) pain disrupts cognitive abilities while in others cognitive performance is improved in the context of pain (A-type). Our previous study provided evidence that the brain reflects these behavioural strategies in that the A group, but not the P group, exhibited attenuation of pain-evoked functional MRI (fMRI) responses in primary and secondary somatosensory cortices (S1, S2), and the anterior insula (aIns) during task performance [76]. However, factors contributing to pain coping strategies (eg, individual characteristics, personality, sensory sensitivity or complexities of brain structure and functional network connectivity) remain unknown.

Pain is of biological importance for survival and thus requires attention [33,60]. Some studies report that pain captures attention and disrupts working memory by reducing performance in cognitive-attentional tasks [9,13,20,21,31,49,53]. Other studies suggest that difficult cognitive tasks reduce pain perception [3,17,30,40,46,47,52,56,64,67,70,71,73,85–87,93]. Accordingly, the A and P characterization helps explain inconsistencies in previous studies.

* Corresponding author. Address: Division of Brain, Imaging and Behaviour—Systems Neuroscience, Toronto Western Research Institute, Toronto Western Hospital, 399 Bathurst St, Room MP14-306, Toronto, Ontario M5T 2S8, Canada. Tel.: +1 (416) 603 5662; fax: +1 (416) 603 5745.
E-mail address: kdavis@uhnres.utoronto.ca (K.D. Davis).

0304-3959/$36.00 © 2013 International Association for the Study of Pain. Published by Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.pain.2013.06.030

Pain and cognitive performance likely share but also compete for mental resources, the outcome of which underlies attentional switch abilities in A- and P-type behaviour. Here, we determined whether these differential effects relate to psychophysical sensitivities to pain, personality factors, brain structure and function. Subjects were assigned to groups on the basis of whether their reaction times (RTs) were faster (A-type) or slower (P-type) in a modified version of the numerical interference task during pain compared to nonpain trials. We predicted that the subject groups are distinguished by their gray and white matter, and connectivity in brain regions and networks involved in pain, attention and salience. To test this, we used voxel-based morphology and cortical thickness analysis to measure gray matter and probabilistic tractography to assess white matter connectivity between gray matter regions that showed group differences. We then used tract-based spatial statistics (TBSS) to investigate white matter integrity group differences in these tracts. Finally, we used resting-state fMRI to determine whether individuals could be distinguished by functional connectivity of sensorimotor and salience resting-state networks.

2. Methods

2.1. Subjects

Eighty healthy right-handed subjects (40 women and 40 men; age range 19 to 36 years, mean ± SD age 24.5 ± 4.9 years) were recruited for the study and provided informed written consent to experimental protocols approved by the University Health Network research ethics board. Each subject underwent 2 experimental sessions. Session 1 included questionnaires, psychophysical tests to determine individuals' thermal and pain sensitivity, temporal summation (TS) of heat pain and a cognitive interference task to categorize subjects into A and P groups on the basis of their behavioural responses. In session 2, structural and functional MRI data were acquired for each subject. The 2 sessions were held between 2 and 12 days apart.

2.2. Questionnaires

Subjects completed the NEO-Five Factor Inventory (NEO-FFI) [19] and the Pain Catastrophizing Scale (PCS) [83].

2.3. Pain sensitivity and tonic heat pain

Heat stimuli were applied to subjects' volar forearm with a 30×30 mm Peltier thermode (TSA-II NeuroSensory Analyzer, Medoc Ltd, Israel) to determine thermal thresholds and to evaluate TS of heat pain.

Details of the testing of cool detection (CD), warm detection (WD), cold pain (CP) and heat pain (HP) thresholds have been previously described [35]. Briefly, 3 consecutive stimulus trials were used for each detection threshold measurement and pain thresholds were measured in 5 consecutive trials on the left volar forearm. For each modality, the baseline temperature was 32 °C. The ramp rates (ie, ascending and descending) for CD and WD were 1 °C/s and consisted of 1.5 °C/s (ascending) and 10 °C/s (descending) for HP and CP. CD and WD had interstimulus intervals of 6 s, and CP and HP intervals were set at 10 s. The order of measurement was kept the same for each subject and consisted of CD, WD CP and then HP. CD and WD thresholds were determined by averaging the last 2 out of the 3 repetitions. CP and HP thresholds were based on the average of the 3 last measures of the 5 trials. A and P group differences for CD, WD, CP and HP were analyzed by univariate analysis of variance (ANOVA).

A modified version of the tonic heat pain model (THPM) introduced by Lautenbacher et al. [57] was used to induce painful stimulation during the cognitive interference task. The THPM consists of repeated pulsating heat stimuli that reach temperatures of 1 °C above the subject's HP threshold. The use of THPM is advantageous because it produces a stable and reliable pain sensation without inducing sensitization or habituation effects [57]. Additionally, stimulation can be repeatedly applied over a prolonged period of time without reaching pain tolerance limits [57]. Here, heat stimuli were applied to the left volar forearm in 60 s blocks and corresponded to the length of 1 block of the cognitive interference task. Each stimulation block started from a baseline of 32 °C. Temperature was then increased from the baseline temperature to the target temperature (ie, 1 °C above the subject's HP threshold) at 7 to 10 °C/s. The temperature was held at this level for 1 s, then decreased to 0.3 °C below the HP threshold and was kept at this temperature for 1 s; rates of 2 °C/s were used to pulsate stimuli between these 2 target temperatures. At the end of each stimulation block, temperature returned to the baseline temperature of 32 °C with rates of 7 to 10 °C/s. We purposely avoided collecting pain intensity ratings during and after the cognitive task to prevent subjects from diverting their attention towards the pain stimulus, which would have biased their behavioural during the task.

Next, TS of heat pain was assessed on the right volar forearm. The baseline temperature was set to 32 °C, and then 10 consecutive 48 °C heat pulses were delivered with an interstimulus temperature of 40 °C at 0.5 Hz and fixed ramp rates of 10 °C/s. Subjects were instructed to rate their pain intensity after each heat pulse on a verbal numerical rating scale that ranged from 0 to 100 (0 = no pain, 100 = worst pain imaginable). For each subject, TS of heat pain was evaluated in 4 consecutive blocks that were separated by 60-s intervals. For TS analysis, the first run was considered as practice run and was discarded from further analysis. To investigate subjective pain intensity increases over the course of the 10 delivered suprathreshold heat pulses, the percentage change of the last heat pulse compared to the first heat pulse was calculated for each run separately, and percentage changes were then averaged over the last 3 stimulation blocks. Between-group effects of TS of heat pain were statistically evaluated by ANOVA.

2.4. Cognitive interference task

In our previous study [76], the A/P classification was based on the Stroop interference task. Because this task typically produces small RT differences (ie, a few milliseconds), here we wished to develop a more robust task in which larger RT differences could be used for a clearer classification into A-and P-types. Therefore, in the present study, a modified version of the numerical interference task [32,92] was used to separate participants into the P- and A-type groups. Our preliminary results for the numerical interference task revealed large RT differences between task conditions that were based on task congruency (ie, >100 ms RT difference between task conditions). The numerical interference task was modified to increase difficulty and thus amplify RT differences between task conditions, allowing for easier subject classification. Subjects viewed a screen that displayed 3 vertically aligned boxes, each containing digits between 1 and 9 (Fig. 1A). Two task conditions varied in difficulty based on congruency. In the easier Value (V) Task, subjects had to determine the highest value of digits across the 3 boxes (dominant information; correct response was "4" in the example shown in Fig. 1A, top). In the more difficult Number (N) Task, subjects were instructed to determine the greatest number of digits across the 3 boxes (nondominant information; correct response was "8" in the example shown in Fig. 1A, top). Subjects entered their responses using a numeric keypad with their right hand and were instructed to respond as quickly as possible but