Experimental Brain Research (2020) 238:321–332
https://doi.org/10.1007/s00221-019-05715-8

RESEARCH ARTICLE

Effects of chronic pain history on perceptual and cognitive inhibition

Mark Hollins[1] · **Chloe P. Bryen**[1] · **Dillon Taylor**[1]

Received: 22 August 2019 / Accepted: 18 December 2019 / Published online: 6 January 2020

Abstract
Measures of sensory and cognitive inhibition were obtained from university students with and without a history of chronic pain. The form of sensory inhibition measured was diffuse noxious inhibitory controls (DNIC), the capacity of a painful stimulus to reduce the subjective intensity of a second stimulus delivered to a remote body site. To measure cognitive inhibition, the Stroop effect was used. Participants with a history of chronic pain showed less DNIC (i.e., less sensory inhibition) than the healthy controls, but had a smaller Stroop effect (indicating greater cognitive inhibition). The fact that chronic pain history is associated with opposite changes in these two measures casts doubt on the view that the two inhibitory processes are related. Scores on each experimental measure were equivalent in pain-history subjects with ongoing chronic pain and those whose chronic pain had resolved. This equivalence suggests that chronic pain in childhood or adolescence may have lingering effects on sensory and cognitive inhibition.

Keywords Chronic pain · DNIC · HNCS · Inhibition · Pain history · Stroop effect

Introduction

Chronic pain is associated with a variety of disturbances of perception and cognition, including widespread lowering of pain threshold (Sarlani and Greenspan 2003), enlarged nociceptive reflex receptive fields (Neziri et al. 2010), disturbed visual perception of pain-relevant biological motion (Lussanet et al. 2012), impaired emotional decision making (Apkarian et al. 2004), and hypervigilance-related perceptual amplification (Hollins et al. 2009; McDermid et al. 1996). Perhaps the disturbance that has received the most attention in recent years is reduced effectiveness of heterotopic noxious conditioning stimulation (HNCS). HNCS is an experimental paradigm in which the perceived intensity of a cutaneous test stimulus is reduced when a strongly noxious "conditioning" stimulus is presented to a remote body site; it has been demonstrated under a wide variety of experimental conditions (Pud et al. 2009).

Communicated by Melvyn A. Goodale.

✉ Mark Hollins
mhollins@email.unc.edu

[1] Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA

DNIC: an example of sensory inhibition

Willer et al. (1984) showed that a key mechanism underlying the effect of HNCS is diffuse noxious inhibitory controls (DNIC), an inhibitory spino-bulbo-spinal loop originally discovered in anesthetized rats by Le Bars et al. (1979).

DNIC involves suppression of activity in wide dynamic range (WDR) neurons in the dorsal horn of the spinal cord (Le Bars et al. 1979), so characterization of this inhibitory process requires understanding of WDR response properties. These neurons respond to both thermal and mechanical stimuli, but with an important difference: in the case of thermal stimuli, WDR neurons respond almost exclusively to noxious levels of stimulation (Khasabov et al. 2001), but with mechanical stimuli they respond to both noxious *and innocuous* levels of stimulation. It is this responsivity to signals from both nociceptors and low-threshold mechanoreceptors (LTMs) that gives WDR neurons their name. Importantly, Le Bars et al. (1979) showed that DNIC reduces the response of WDR cells to signals from LTMs as well as signals from nociceptors.

It should be noted that in experiments using an HNCS paradigm, reduction in the perceived intensity of a test stimulus may reflect factors other than, or in addition to, DNIC. Specifically, attentional shifts caused by the conditioning stimulus are sometimes thought to play a role. Since

attention perceptually amplifies painful stimuli (Miron et al. 1989), a conditioning stimulus that draws attention away from a noxious test stimulus could reduce its subjective intensity. This may account for the modest effect of HNCS sometimes seen with a non-painful thermal test stimulus (Lautenbacher et al. 2002), which does not activate WDR neurons and is, therefore, unaffected by DNIC. However, in the present study, in which mechanical test stimuli were used, we will for simplicity refer to the effect of HNCS as DNIC, with the acknowledgment that attentional factors may also be contributing to some degree.

Chronic pain and DNIC

DNIC has been reported to be deficient in patients with fibromyalgia (Julien et al. 2005; Kosek and Hansson 1997; Lautenbacher and Rollman 1997; but see Staud et al. 2003, 2004), chronic tension-type headache (Pielsticker et al. 2005; Sandrini et al. 2006), migraine (Sandrini et al. 2006), irritable bowel syndrome (King et al. 2009; Piché et al. 2011; Wilder-Smith et al. 2004), temporomandibular disorder (King et al. 2009; but see Garrett et al. 2013), osteoarthritis (Arendt-Nielsen et al. 2010; Graven-Nielsen et al. 2012; Kosek and Ordeberg 2000), chronic pancreatitis (Bouwense et al. 2013; Olesen et al. 2010), and other chronic pain conditions (see meta-analysis by Lewis et al. 2012). While there is evidence that the extent of DNIC impairment differs across clinical conditions (Gerhardt et al. 2017), its occurrence in so many pain syndromes suggests that a convenience sample of people with self-reported chronic pain is likely to show less DNIC than a healthy control sample.

Weakened DNIC circuitry may both contribute to and result from chronic pain, but the mechanisms underlying such interactions are not understood. One possibility is that a deficiency of DNIC might allow pain signals to proceed relatively unchecked to higher levels of the neuraxis, contributing to supraspinal changes that are an important part of the chronic pain state. Consistent with this possibility, the amount of DNIC shown by patients before major surgery has been found to (negatively) predict the likelihood that chronic pain will develop after surgery (Yarnitsky et al. 2008).

In addition, long-term nociceptive input in a chronic pain patient could damage DNIC circuitry through overuse, rendering subsequent pain less susceptible to modulation (Coggeshall et al. 2001; Inquimbert et al. 2018). Alternatively, chronic nociceptive input might interfere with DNIC dynamically, by saturating its circuitry (Granot et al. 2008) so that an experimental conditioning stimulus would not trigger much additional inhibition. In this situation, the magnitude of DNIC would be reduced even if the underlying neural machinery were functioning normally. Consistent with this possibility, DNIC is sometimes restored to normal strength if a peripheral source of chronic pain signals is eliminated, for example by joint replacement (Graven-Nielsen et al. 2012; Kosek and Ordeberg 2000).

Stroop: an example of cognitive inhibition

An important question is whether an impairment of DNIC is an isolated abnormality of the pain system, or reflects a more general weakening of central inhibitory mechanisms, such as posited by Marouf et al. (2014) to occur as part of normal aging. Their elderly participants showed not only a failure of DNIC (confirming Edwards et al. 2003), but also an increased Stroop (1935) effect, measured using the color-word task. In this paradigm, the subject is asked to name, on each of a series of trials, the color in which the name of a different color is visually presented (e.g., the subject must respond "red" when the word blue is presented in red letters). The gradual increase in the Stroop effect with age is a well-established phenomenon (Bugg et al. 2007); its etiology is complex (Peng et al. 2017), but a key contributor is an age-related decline in the ability to inhibit responses to unwanted information (Augustinova et al. 2018).

In contrast to the findings of Marouf et al. (2014) regarding the effects of aging, a generalized weakening of cognitive inhibition in chronic pain patients (regardless of age) seems unlikely, given that most studies have found the Stroop effect to be of normal magnitude in chronic pain patients (Apkarian et al. 2004; Oosterman et al. 2012; Suhr 2003; Veldhuijezen et al. 2012). However, a test of this finding's applicability to young adults is warranted, given that participants in most earlier studies were in middle age or beyond.

Goals of the present study

In the present study, we seek to increase understanding of the reduced DNIC found in many chronic pain conditions by asking two questions: first, is the reduction part of a widespread weakening of inhibitory processes, or is it confined to the pain system? And second, is the reduced level of DNIC a long-term impairment, or only a temporary (e.g., dynamically maintained) one?

To settle the first question, we measured both Stroop performance and DNIC in participants with and without a history of chronic pain. The inhibition required by the Stroop task is not a low-level process, but a complex cognitive ability—an executive function—to manage information. Abnormal Stroop scores could, therefore, reflect either an impairment confined to inhibitory processes, or a more general compromising of executive function. To distinguish between these possibilities, we also administered the operation span (Ospan) task, which focuses on other executive

functions: working memory and task switching (Turner and Engle 1989; Unsworth et al. 2005).

To address the second question—whether the impairment in DNIC often found in chronic pain patients can continue to occur even if the chronic pain resolves—we compared the effects of HNCS in two groups of individuals with a history of chronic pain: those whose pain had resolved, and those who still had chronic pain at the time of the study. If chronic pain damages the neural circuitry that produces DNIC, this inhibitory process will remain weak even if the individual has otherwise recovered from the chronic pain condition.

In the present study we chose to use cutaneous pressure as a test stimulus, for two reasons. First, the aching, protean quality of pressure discomfort resembles some types of clinical pain. While gentle pressure activates only LTMs, causing tactile sensations, moderate pressures that are above nociceptor threshold can evoke unpleasant but non-painful sensations such as pricking (Van Hees and Gybels 1981). Still higher pressure can evoke frank pain. Because we used a wide range of forces, the test stimuli became increasingly unpleasant and sometimes painful as force increased.

The second reason we used mechanical test stimuli is that WDR neurons respond to these stimuli at both innocuous and noxious intensities (Price and Dubner 1977), potentially enabling DNIC to affect perception of both painful and non-painful levels of stimulation. The use of pressure as a test stimulus therefore provided us with the opportunity to examine this form of sensory inhibition over a wide range of test stimulus intensities.

Methods

Participants

The participants were 80 undergraduate university students enrolled in an introductory psychology class, who received research credits for participating. Subjects signed up for the study online and came to the laboratory for a single session lasting just under 90 min. Recruitment materials indicated that the study concerned pain (especially chronic pain) and memory, but that chronic pain was not a requirement. Subjects gave written informed consent and were debriefed at the end of their participation. All aspects of the study were approved in advance by the Institutional Review Board of the University of North Carolina at Chapel Hill.

Exclusion criteria were: (1) age less than 18 or more than 25; (2) current enrollment in a course taught by the first author; (3) diabetes; (4) urticaria, Raynaud's disease, or a peripheral vascular disease (conditions that could be affected by the cold-water conditioning stimulus); (5) a neurological impairment; (6) surgery, nerve damage, or a current injury such as a cut or bruise, on either hand or forearm; and (7) color blindness or abnormal color vision (because of the Stroop test).

Materials and procedure

Questionnaires

Subjects first completed questionnaires about their current and previous experiences with pain, including chronic pain. We explained to participants that chronic pain (CP) is pain that lasts for 3 months or more, occurring daily or almost every day. This is similar to the definition of chronic pain as "pain that persists or recurs for more than 3 months" recently adopted by the International Association for the Study of Pain (Treede et al. 2019). Subjects who reported a history of chronic pain indicated when it had occurred, using a scale developed earlier in our lab (Mullis 2011) that consisted of a row of labeled boxes representing the years of the participant's life, from birth to the present. Subjects were asked to check every box corresponding to an age at which chronic pain had been present, and were also asked whether it was still occurring. Forty-one of the participants indicated that they had experienced chronic pain at some point in their lives, and of these, 19 individuals still had chronic pain at the time of the study.

In only a few cases were subjects able to provide a formal medical diagnosis for their chronic pain. When asked where on the body they had experienced pain, many indicated the extremities and the back, and mentioned injuries, suggesting a predominance of musculoskeletal conditions.

Regarding current pain, all participants were asked to rate, on a 0–100 scale, both the intensity of any pain they were experiencing at the present moment ("right now"), and the average intensity of any pain they had experienced during the previous 2 weeks.

The Pennebaker Inventory of Limbic Languidness (PILL: Pennebaker 1982) was also administered. This measure of hypervigilance has been used to establish the occurrence of perceptual amplification in people with some idiopathic chronic pain conditions (Hollins et al. 2009; McDermid et al. 1996). It asks respondents to indicate how often they experience each of 54 common symptoms, such as running nose or hot flashes. Reporting at least weekly occurrence of many symptoms suggests that the respondent is hypervigilant.

To assess the potential value of their use in future studies, 3 additional questionnaires were given to the last 48 participants (28 with a chronic pain history and 20 controls). These were the Body Vigilance Scale (BVS: Schmidt et al. 1997), the Pain Vigilance and Awareness Questionnaire (PVAQ: McCracken 1997), and the Pain Catastrophizing Scale (PCS: Sullivan et al. 1995). Since these additional questionnaires were not given to all participants, scores on them are not included in this report.

Finally, all subjects completed a brief demographics form (age, sex, race, handedness).

Ospan

The operation span task (Ospan) is a test of executive function, especially working memory. It requires subjects to carry out two cognitive tasks concurrently, specifically solving mental arithmetic problems while also keeping track of letters (Turner and Engle 1989). We used a computer-administered version of this task developed by Unsworth et al. (2005). The program runs on the Inquisit platform (Millisecond Software, Seattle).

As the task begins, an arithmetic problem is presented and then a possible answer; the subject must decide whether this answer is correct. Once the subject responds, a letter is presented. These steps are repeated 3–7 times, after which the subject is asked to recall (by selecting from an array) all the letters that were presented, in order. Many such trials are administered, and the subject's Ospan score is the total number of letters in trials for which every letter was correctly recalled.

Stroop

The Stroop color-word test (Stroop 1935) was used as a measure of the ability to cognitively suppress task-irrelevant information. On a computer screen, subjects viewed a series of 60 letter strings presented in color (red, green, blue, yellow, or brown) against a gray background. The subject's task was to say aloud, as quickly as possible, the color in which each of the letter strings was presented. The experimenter recorded the total time required by the subject, and noted any errors made.

The task was carried out twice. In the control condition, all the letters were Xs, so that the subject's task was relatively easy. In the experimental ("Stroop") condition, the letter strings were the words red, green, blue, yellow, and brown. Each color name was always presented in a non-matching color: for example, the word *red* was always presented in either green, blue, yellow, or brown. The two conditions were carefully matched in physical properties such as the number of letters in a string (ranging from 3 to 6) and the number of times each color was used in the array (12). Sixteen different versions of each array were used, to ensure that results would not depend on the particular order of stimuli within an array. The two conditions were carried out in random order. The stimuli were the same ones used by Harper and Hollins (2012).

The magnitude of the Stroop effect was calculated by subtracting a subject's total time in the control condition from the (almost always greater) time required in the experimental condition. Errors were infrequent and therefore not analyzed.

DNIC experiment

To examine DNIC, we measured the ability of a frankly painful conditioning stimulus (cold pressor) to reduce the perceived intensity of a localized pressure test stimulus to the contralateral arm.

The test stimulus was a vertical cylindrical rod (tip diameter 5 mm) that pressed down on the dorsal surface of the subject's right forearm, midway between wrist and elbow. Within a stimulus series, six levels of force ranging in 200 g steps from 77 to 1077 g were delivered to the subject, in random order. The stimuli and their method of delivery are the same as those used by Hollins et al. (2009). Each stimulus was gradually lowered onto the skin over the course of about 1 s, left in place for 15 s, and then gently lifted off. After a stimulus was removed, subjects rated the intensity of the sensation it produced on a 0–100 scale, where 0 meant "no sensation" and 100 signified "the most intense sensation imaginable." Subjects then categorized the stimulus as painful, unpleasant but not painful, or neutral (i.e., neither pleasant nor unpleasant). Finally, subjects rated the unpleasantness of the sensation on a scale ranging from 0 ("not at all unpleasant") to 100 ("the most unpleasant sensation imaginable").

Throughout a series of test stimuli, the contralateral (left) hand was immersed in a 10-liter cooler of water. Air bubbled through an air stone continually circulated the water. Water temperature was measured with an electronic thermometer (Model 421,502, Extech Instruments Corp., Nashua, NH, USA) with a K bead thermocouple. In the control condition, the water was at 32 °C and produced little or no thermal sensation. In the experimental ("cold pressor") condition, the water was adjusted to 6 °C, and produced frank pain. A plastic partition with holes divided the cooler into a section for the subject's hand, and a section in which (in the experimental condition) ice was added to the water. The control condition was always carried out prior to the experimental condition, so that any aftereffects of the cold water would not affect the control condition data. In both conditions, subjects lowered their hand into the water up to the crease of the wrist, prior to the delivery of the first test stimulus, and left it in the water until instructed by the experimenter to remove it at the end of the series of test stimuli (no more than 5 min). Subjects were told that they were free to remove their hand from the water at any time; four did so early in the cold-water test series, after rating just one or two pressure stimuli. None of these four had a chronic pain history. Cold-water data could not be obtained on another participant because of an apparatus malfunction. We thus obtained complete DNIC data on 75 individuals.

The amount of DNIC was computed by subtracting ratings of sensation intensity and unpleasantness in the experimental condition from those in the control condition.

Results

Pain history

The 80 participants ranged in age from 18 to 23 years ($M = 19.1$; SD = 1.1). Fifty were female.

Forty-one of the participants reported having had chronic pain (defined as pain that was experienced daily or almost daily for three months or more) at some point in their lives, and are referred to as the chronic pain history (CPH) group. The 39 subjects without a history of chronic pain constituted the healthy control (HC) group. The high percentage of subjects in the chronic pain history group (51%) was presumably a result of the fact that recruitment materials that mentioned a history of chronic pain as a focus of the study (although not a requirement for participation), thereby making it of interest to those with such a history.

Because there is evidence that DNIC is less effective in women than men (Popescu et al. 2010), we examined the possibility that females and males made up different proportions of the pain history and control groups. Female participants constituted 56.1% of the pain history group, and 69.2% of the control group; this difference was not significant, $X^2(1) = 1.47$, $p = 0.225$. The difference in age between the chronic pain ($M = 19.1$ years, SD = 1.3) and control ($M = 19.2$ years, SD = 1.0) groups was likewise nonsignificant, $t(78) = 0.124$, $p = 0.902$.

The age at which, by self-report, subjects' chronic pain began averaged 15.3 years ($SD = 4.1$). One individual reported knowing that he had extended pain in the first year of life, during recovery from surgery, but that he didn't "remember it very well." For all others, the reported age at which chronic pain began ranged from 8 to 21. Just over half the members of the pain history group ($n = 22$) reported that their chronic pain had resolved prior to the study; the other 19 still had chronic pain at the time of their participation.

Current pain

The distributions of current pain scores, both those indicating pain intensity at the outset of a subject's participation ("right now" scores), and those reflecting the average intensity of any pain experienced over the previous 2-week period, showed a strong positive skew: For example, "right now" scores ranged from 0 to 60 on the 0–100 pain intensity scale, but the median of the distribution was 0, and only eight of the scores were above 10. Because current pain scores were not normally distributed, a nonparametric instrument, the Mann–Whitney *U* test for independent samples, was used in all tests reported in this section.

To determine whether ongoing current pain during the experimental procedures could perhaps explain any differences in performance that were found between the chronic pain history group and the healthy control group, the "right now" pain scores of the two groups were compared; they were not significantly different ($p = 0.269$), and the median (Mdn) score for each group was 0.

A contrasting result was obtained when scores reflecting average pain over the 2-week period preceding the study were examined: Scores for participants with a chronic pain history (Mdn = 10) were higher than those for the healthy controls (Mdn = 5), $p = 0.004$. Importantly, there was a significant difference between the members of the chronic pain history group who reported current chronic pain (Mdn = 20), and those who did not (Mdn = 6), $p = 0.003$; moreover, the former subset of CPH participants differed significantly from the HC group ($p < 0.001$), while the latter subset, i.e., participants who had previously had chronic pain but no longer did, were statistically indistinguishable from the HC group ($p = 0.423$).

Taken as a whole, these data are consistent with the view that participants with ongoing chronic pain will experience substantial pain over the course of a 2-week period, but not necessarily at a specific time (i.e., the time of their research participation).

DNIC experiment

Painfulness of the conditioning stimulus

DNIC analysis is limited to the 75 participants who provided complete data sets, rating the sensations they experienced from all six weighted rod test stimuli in the presence of both thermally neutral (32 °C) and cold (6 °C) conditioning stimuli. In addition, once they had removed their left hand from the water, they rated its painfulness using separate 0–100 scales for intensity (from "no pain" to "the most intense pain imaginable") and unpleasantness (from "not at all unpleasant" to "the most unpleasant pain imaginable").

Pain intensity of the neutral water was rated as 0 by most participants in both the pain history group (39/41) and the control group (29/34). Because the distributions of these scores for both groups had a strong positive skew, a nonparametric test, the Mann–Whitney *U* test, was used to compare them. There was no evidence of a difference between groups, $p = 0.725$. Results for pain unpleasantness of the neutral water were likewise equivalent in the two groups, $p = 0.072$.

In contrast, the cold water elicited strong pain ratings from subjects in both groups. (Pain ratings for the water were not obtained from one subject in the control group, due to experimental error.) Pain intensity ratings were similar in the chronic pain history ($M = 53.46$; SD = 21.31) and control ($M = 47.64$; SD = 23.92) groups, and the difference between

them was not significant, $t(72) = 1.107$, $p = 0.466$. Results for the pain unpleasantness ratings of the cold water showed a similar pattern: ratings by the pain history group ($M = 64.37$; SD = 20.17) and the control group ($M = 54.64$; SD = 24.97) were statistically equivalent, $t(72) = 1.855$, $p = 0.118$.

Classification of test stimuli

Participants classified each test stimulus as painful, unpleasant but not painful, or neutral (defined as neither pleasant nor unpleasant). Combined results for all subjects, when the contralateral hand was in 32 °C water, are shown in the upper panel of Fig. 1, where percentages of "painful" and "unpleasant" responses are plotted as a function of the force exerted by the test stimulus. At the lowest force level only 1% of subjects classified the stimulus as painful, but with increasing force, the frequency of "painful" responses gradually increased, reaching 31% at the highest force level.

Compared to these data in the baseline condition, "painful" responses were less frequent when the contralateral hand was in cold water (lower panel in Fig. 1), where only 11% of subjects categorized the test stimulus as painful at the highest force level.

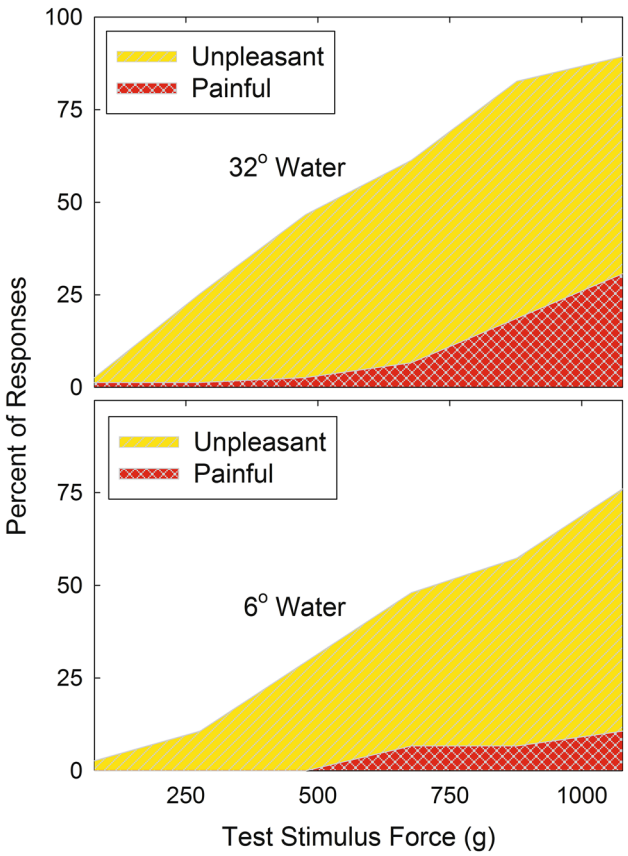

Fig. 1 Subjects' classification of the test stimulus as either painful (crosshatched), unpleasant but not painful (hatched), or affectively neutral (unfilled region), when the contralateral hand was in thermally neutral water (upper panel) or painfully cold water (lower panel). Painful and unpleasant classification responses were less frequent in the cold-water condition, indicating the occurrence of DNIC

Classification response tallies represent an ordinal level of measurement, so nonparametric analysis was used to test for the presence of DNIC. We tabulated for each subject the number of trials, summed across force levels on which he/she classified the sensation from the weighted rod as painful. This was done separately for the cold-water and neutral-water conditions, and results for the two conditions were compared using the Wilcoxon matched-pairs signed-rank test. The effect of condition was highly significant ($p < 0.001$), with painful responses being given less often in the cold-water condition (4.0% of trials) than in the neutral condition (10.2%); thus, for our overall sample, DNIC occurred.

We next carried out the same analysis for the chronic pain history group and the control group separately. The effect of conditioning stimulus temperature on the frequency of "painful" responses was significant in both the healthy control group ($p = 0.003$) and the chronic pain history group ($p = 0.029$), showing the presence of DNIC in both groups. Interestingly, the percentage of trials on which the test stimulus was reported as painful tended to be somewhat higher for the healthy control participants than for the chronic pain history participants in both the neutral condition (13.7% vs. 7.3%) and the cold-water condition (4.4% vs. 3.7%). Although these trends were not significant (Mann–Whitney U tests, both $p > 0.05$), they were directionally consistent with a reviewer's suggestion that chronic pain patients, since they regularly experience strong pain, may be more reluctant than healthy controls to classify a weakly noxious sensation as painful.

"Unpleasant" classification responses were more common than "painful" ones, but followed a similar pattern, rising from 1% of responses at the lowest force level to 59% at the highest. For our overall sample, "unpleasant" responses were significantly more frequent in the neutral water condition than in the cold water condition (Wilcoxon matched-pairs signed-rank test, $p = 0.005$), confirming that DNIC can occur even when test stimulus aversiveness does not rise to the level of frank pain. Separate analyses for the two groups showed the effect of condition to be significant for the chronic pain history group (Wilcoxon, $p = 0.007$) although not for the healthy control group ($p = 0.312$).

In summary, participants' classification responses confirm the occurrence of DNIC in our experimental paradigm. The fact that significant effects of condition (i.e., of water temperature) were found in almost all statistical comparisons suggests that the phenomenon was robust. However, it is not possible to calculate from these ordinal measurements the *magnitude* of reductions in the perceived intensity or unpleasantness of test stimuli in the presence of a noxious

conditioning stimulus. For this it is necessary to turn to the scaling data.

Sensation intensity

To determine whether the perceived intensity of the test stimulus was systematically reduced when the contralateral hand was in pain, and whether such reduction occurred equally in the pain history and control groups, a 2 (water temperature) × 6 (test stimulus force) × 2 (pain history and control groups) mixed-model ANOVA was carried out on sensation intensity ratings. The main effect of water temperature was highly significant, $F(1,73) = 32.65$, $p < 0.001$, intensity ratings of the test stimulus being lower when the contralateral hand was in cold, as opposed to neutral, water. As expected, intensity ratings increased significantly with increasing test stimulus force, $F(5,365) = 89.61$, $p < 0.001$; the interaction of temperature and force was also highly significant, $F(5,365) = 5.11$, $p < 0.001$, in that temperature affected ratings more at high than at low force levels.

Importantly, there was a significant interaction of temperature and group, $F(1,73) = 4.09$, $p = 0.047$, with temperature having less of an effect (i.e., there was less DNIC) for the chronic pain history group than for the control group (see Fig. 2). Neither the main effect of group nor its other interactions was significant (all $p > 0.3$).

To determine whether the reduced effect of temperature on intensity ratings in the pain history group was due to the fact that some of these participants still had chronic pain, we compared the overall strength of DNIC—calculated as the average, across force levels, of the difference in sensation intensity ratings between cold and neutral water conditions—in these two subsets of the CPH group. The amount of DNIC was equivalent in those who currently had chronic pain ($n = 19$) and those whose earlier chronic pain had resolved ($n = 22$), $t(39) = 1.27$, $p = 0.212$ (See Fig. 3).

To further test the equivalence of the two subgroups of the chronic pain history group, we compared their DNIC scores using a Bayesian t test for independent samples (SPSS 25). Assuming unequal variances in the two subgroups, and using a non-informative (Jeffreys) prior, we obtained a Bayes factor of 2.15, which slightly favors the null hypothesis—that there is no difference between subgroups—over the alternative hypothesis. Taken as a whole, the evidence thus favors the view that it is a history of chronic pain that is associated with reduced DNIC, rather than simply current chronic pain.

When the pain-history subgroups were separately compared with the healthy controls, the reduction in DNIC was not significant either for those whose former pain had resolved [$t(54) = 2.00$, $p = 0.051$] or those with current chronic pain, $t(51) = 1.02$, $p = 0.311$.

Sensation unpleasantness

Numerical unpleasantness ratings of the test stimulus were qualitatively similar to intensity ratings and were analyzed in the same way. A 2 (water temperature) × 6 (test stimulus force) × 2 (pain history and control groups) ANOVA showed that the main effect of water temperature was highly significant [$F(1,73) = 41.07$, $p < 0.001$], the weighted rod being perceived as less unpleasant when the contralateral hand was in cold, as opposed to neutral, water. As expected, unpleasantness rose as force increased, [$F(5,365) = 64.32$,

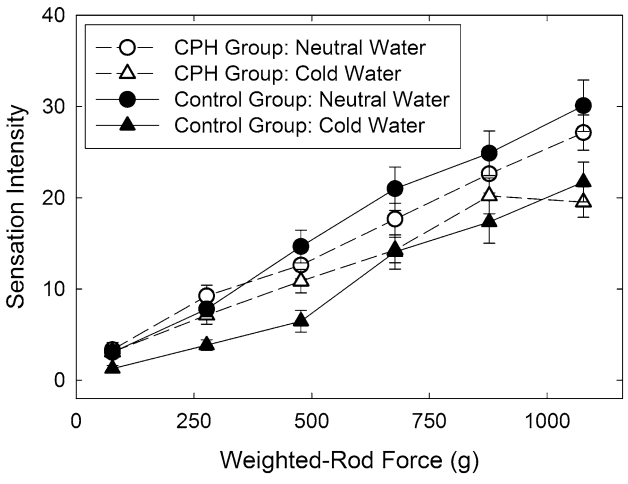

Fig. 2 Mean intensity of the sensation produced by the weighted rod is shown as a function of stimulus force. Ratings were lower when the contralateral hand was in painfully cold water (triangles) than when it was in thermally neutral water (circles). The effect of temperature was greater in the control subjects (filled symbols) than in those with a history of chronic pain (open symbols). Error bars represent ± 1 SEM

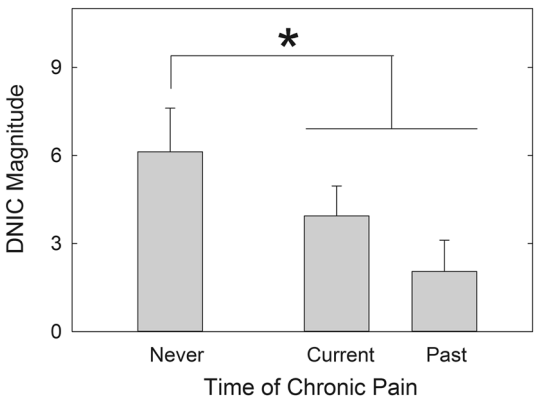

Fig. 3 Average DNIC is shown for members of three groups of participants: healthy controls; those with chronic pain extending up to the time of the study; and those with past chronic pain that had resolved. DNIC is significantly greater for the controls than for the two chronic pain groups combined. Error bars indicate 1 SEM

$p < 0.001$], and water temperature had a greater effect on unpleasantness at greater levels of force, $F(5,365) = 11.81$, $p < 0.001$. The interaction of temperature and group was not significant, $F(1,73) = 2.74$, $p = 0.102$. No other terms approached significance (all $p > 0.5$).

Stroop task

Stroop scores were calculated as the difference, in seconds, between the total time subjects required to complete the two tasks (Stroop condition minus control condition). Scores for the chronic pain history group ($M = 12.25$; SD = 5.61) were significantly lower than scores for the control group ($M = 15.21$, SD = 7.16), $t(78) = 2.06$, $p = 0.042$. In other words, participants with a history of chronic pain were on average more adept at suppressing task-irrelevant information than members of the control group.

To determine whether the better Stroop performance of those in the pain history group was due to the fact that some of them still had chronic pain, we compared current chronic pain individuals ($n = 19$) with those whose earlier chronic pain had resolved ($n = 22$). (See Fig. 4.) The Stroop scores of those who still had CP at the time of the study ($M = 11.74$; $SD = 6.12$) were statistically equivalent to the scores of those who did not ($M = 12.70$, SD = 5.25), $t(39) = 0.542$, $p = 0.591$.

To further test this equivalence, we carried out a Bayesian t test for independent samples, assuming unequal variances and using a non-informative (Jeffreys) prior. This test yielded a Bayes factor of 3.81, constituting substantial evidence (Kass and Raftery 1995) for the null hypothesis. What was demonstrably relevant to the enhanced Stroop performance of our college-age subjects was having had chronic pain at some point in life, whether or not it continued to the present.

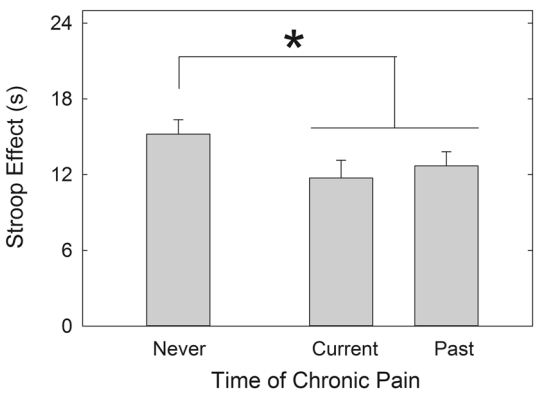

Fig. 4 Average Stroop effect is shown for members of three groups of participants: healthy controls; those with chronic pain extending up to the time of the study; and those with past chronic pain that had resolved. The Stroop effect is significantly greater for the controls than for the two chronic pain groups combined. Error bars indicate 1 SEM

When the subgroups were considered separately, Stroop scores of neither the current chronic pain subgroup nor the former chronic pain subgroup were significantly different from those of the healthy controls ($p = 0.075$ and $p = 0.155$, respectively).

A subject's Stroop score was not related to the strength of his/her DNIC, $r(75) = 0.064$, $p = 0.584$.

Ospan task

Ospan scores were calculated as the number of recalled letters, summed across those trials on which all letters were correctly recalled in the correct order. Scores were compared for participants with ($n = 41$) and without ($n = 39$) a history of chronic pain. Scores for the chronic pain history group ($M = 46.63$; SD = 15.80) and the control group ($M = 44.97$; SD = 12.68) were not significantly different, $t(78) = 0.517$, $p = 0.607$. The results do not support the possibility that working memory (or more generally, executive function) is compromised in those with a history of chronic pain.

Hypervigilance

PILL scores were equivalent in the chronic pain history and control groups [$t(78) = 1.09$, $p = 0.279$], and were not correlated with Ospan scores [$r(80) = 0.053$, $p = 0.643$], DNIC scores [$r(75) = -0.050$, $p = 0.673$], or Stroop scores [$r(80) = -0.013$, $p = 0.909$].

Discussion

The overall purpose of the present study was to increase understanding of the well-established association between chronic pain and an impairment in DNIC, a key endogenous pain control process.

DNIC and chronic pain history

People with chronic pain have, by definition, suffered from it for at least 3 months, and, therefore. may be said to have a chronic pain history; in many cases the pain has lasted much longer. We asked a college-age sample of participants to report their experiences of chronic pain, whether past or present, and we compared the strength of DNIC in those with and without a chronic pain history. Although our study used a convenience sample, and depended on self-report regarding chronic pain history—factors that might be thought likely to increase variability and cloud interpretation—the results demonstrated that DNIC was reduced in the pain history group, compared to the control group. The fact that our pain history group was not restricted to a particular clinical condition confirms the

generally accepted view (e.g., Lewis et al. 2012) that DNIC impairment is a widespread characteristic of chronic pain, though perhaps present to a greater degree in some conditions than others (Gerhardt et al. 2017).

However, the data raised the further question of whether the reduction in DNIC seen in the chronic pain history group depended, in a dynamic way, on their current and recent pain, or whether it was a gradually-developed result of their long experience with pain. To decide between these possibilities we compared participants with current chronic pain with others having a history of chronic pain that had since resolved. The data indicated that DNIC was equally weakened (compared to healthy controls) in those whose chronic pain had, and those in whom it had not, resolved. This finding suggests that a period of chronic pain, even one earlier in life, is associated with an impairment of DNIC.

The fact that DNIC did not normalize in participants who had otherwise recovered from chronic pain may appear to be in conflict with the results of studies showing that it does normalize in osteoarthritis patients whose chronic pain is eliminated by joint replacement surgery (Graven-Nielsen et al. 2012; Kosek and Ordeberg 2000). However, the participants in those studies were considerably older than our subjects, and their arthritis pain typically began when they were well into adulthood; chronic pain may have a more lasting effect on neural mechanisms underlying DNIC in young individuals than it does in older ones.

Stroop performance and chronic pain history

Another way in which we explored the link between chronic pain history and impaired DNIC was to determine its specificity. DNIC is only one of a large number of inhibitory processes, sensory and cognitive, that have been experimentally measured. We asked whether chronic pain history is associated with a decline in inhibitory processes generally, or only with a decline in DNIC.

To address this question we also administered the Stroop (1935) color-word test to our sample. This task is widely believed (e.g., Marouf et al. 2014) to tap a cognitive process, response inhibition; it is an example of inhibition differing on several dimensions from DNIC. We expected either that Stroop inhibition would be of normal magnitude in chronic pain patients (indicating that the two forms of inhibition are unrelated), or that it would be weakened, just as DNIC is (indicating a widespread association between chronic pain history and impaired inhibition). To our surprise, we found that people with a chronic pain history had *stronger* Stroop inhibition (i.e., a smaller Stroop effect) than the healthy controls.

This finding indicates that, in our sample of young adults, those with a history of chronic pain are more skilled at suppressing or ignoring unwanted perceptual information than those with no history of chronic pain. Heightened selective attention (i.e., cognitive inhibition) may be a skill that some chronic pain patients develop because it enables them to reduce the disruption of everyday life by the distracting effect of pain. Once learned, this skill could be applied to other types of distractors, e.g. color names in the Stroop task. Importantly, it appears to be a skill that, once developed, is not readily lost even if the original reason for it—chronic pain—no longer exists.

Our results differ from those of earlier studies (Apkarian et al. 2004; Oosterman et al. 2012; Suhr 2003; Veldhuijezen et al. 2012) in which no significant difference was found between chronic pain patients and healthy controls on the Stroop color-word task. The most salient difference between this earlier work and our own is that participants in the earlier studies were considerably older than those in our college sample. The Stroop effect increases with age over the range 20–89 years (Bugg et al. 2007), due in large part to an age-related decline in the ability to inhibit responses to unwanted information. It would not be surprising if the potential to learn this cognitive ability, reinforced (as we have suggested) by the relief from chronic pain that it produced, were likewise greatest in young adulthood.

As was the case with DNIC, no difference in Stroop scores was found between pain history subjects whose chronic pain had resolved, and those in whom it had continued up to the time of the study.

Enhanced Stroop performance in our pain history subjects was not part of a change in overall executive function, since Ospan scores, which reflect working memory and task switching, were not affected.

Stroop inhibition and DNIC are unrelated

The contrast between two of our major findings—*increased* inhibition in the pain history group shown by reduced Stroop scores, and *decreased* inhibition shown by their reduced DNIC scores—indicates that these two concomitants of chronic pain are not manifestations of a global change in inhibition, such as has been reported to occur with aging (Marouf et al. 2014). This is consistent with the fact that DNIC and Stroop scores were uncorrelated across individuals in the present study. The evidence thus indicates that these two inhibitory processes are not related.

Conclusions

In summary, the results of the present study indicate that a history of chronic pain is associated with a level of DNIC below that of healthy control subjects. DNIC was equivalent in individuals whose chronic pain continued up to the present, and those who had chronic pain earlier in life that was resolved by the time of the study. This suggests that aftereffects of previous chronic pain may be one of several factors leading to a reduction in DNIC. However, scores on the Stroop color-word task showed, surprisingly, that the type of inhibition measured by this cognitive task is stronger than normal; DNIC inhibition and Stroop inhibition are, therefore, unrelated.

While our findings are clear, they point to the need for further research, developed along at least two lines. First, our classification of participants depended on self-report, including reports of pain experienced years ago; it would be desirable to have medical records or other contemporaneous documentation of this earlier pain. Second, our study is a cross-sectional one; establishing cause-and-effect relationships between parameters of chronic pain history and experimental measures would require a more longitudinal approach. Despite its limitations, however, the present study has important implications for our understanding of chronic pain, and the complex and sometimes unpredictable ways in which it interacts with perception and cognition.

Acknowledgements The authors are grateful to Zack Fisher for advice on Bayesian analysis, and to Samuel Brotkin for laboratory assistance. This study was supported by a Lindquist Award from the UNC College of Arts and Sciences, and by a Dunlevie Honors Research Award to DT.

Author contribution All authors contributed to the study conception and design, to preparation of materials, and to data analysis. Data Collection was carried out by CB and DT. The first draft of the manuscript was written by MH; all authors commented on drafts of the manuscript, and read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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