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Cognitive Impairment in Chronic Pain

Pain and Cognition: Interrelations

This issue of *Pain: Clinical Updates* addresses the effects of chronic pain on cognitive function. A literature search on the combination of “pain” and “cognition” identifies 1,200 items in the Medline and PsychInfo databases alone. This substantial but not unexpected result speaks to the interest of many researchers and clinicians in the interrelations of these two areas. Our own survey of this literature indicates five major themes: (1) cognitive modulation of the occurrence and maintenance of pain, such as the impact of learning, expectancy, beliefs, and attitudes; (2) cognitively based therapies for pain;¹ (3) cognitive sequelae of pain treatment, including the impact of opioids or deep brain stimulation on cognitive performance; (4) the influence of differential levels of cognition on pain assessment and treatment, especially in the elderly or in patients with dementia; and (5) effects of pain on the content and the process of cognition. About 5% of the literature on pain and cognition addresses this last topic, which is the focus of the present survey. Further restricting our attention to chronic pain excludes transient, acute pain as well as experimentally produced (i.e., laboratory) pain. This issue of *Pain: Clinical Updates* emphasizes cognitive functioning rather than cognitive content such as beliefs concerning pain that underlie coping with chronic pain and thereby may influence its course.

The Importance of the Effects of Pain on Cognition

Several authors^{2,3} have emphasized two key reasons to elucidate the effects of chronic pain on cognition. First, if these effects are even in part negative, their impact could be substantial. Such negative effects may exacerbate suffering⁴ as well as anxiety (including specific worries about brain dysfunction as a consequence of pain),⁵ depression,⁶ and restriction of activities—all of which diminish an already compromised quality of life in patients with chronic pain.⁷ Second, cognitive impairment in patients with chronic pain could restrict patients’ effectiveness in communicating their pain symptoms and constrain application of cognitively based treatments.¹

To these concerns we would add that as long as cognitive symptoms are not assessed, they are unlikely to be treated. Moreover, precise information about the cognitive impact of pain could shed light on brain mechanisms that mediate both pain and cognition, thereby pointing the way toward new treatment strategies.

Difficulties in Studying Pain-Cognition Interactions

A recent comprehensive review of the effects of chronic pain on neuropsychological function⁸ described a number of research findings indicative of impaired function in patients with chronic pain, particularly on tests of attentional

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capacity, processing speed, and psychomotor speed. However, such findings must be considered as merely suggestive because of several fundamental problems hampering any attempt to clarify the impact of pain on cognition. One major problem is the difficulty of untangling the cognitive effects of chronic pain from the effects of neurological disorders that in many cases are the cause of the pain. The onset of such disorders may precede the emergence of pain, as in the case of older persons⁹ who suffer from conditions ranging from multi-infarct or nutritional dementias through Alzheimer's disease. The preexisting disorder may well magnify the effects of chronic pain upon preexisting cognitive deficits. Equally problematic is the case of new neurological disorders due to brain injury concurrent with the onset of chronic pain. Traumatic brain injuries of at least a mild degree are common in situations such as accidents or emergency surgery, when acute pain begins the transition into persistent pain. Here again, the neurologically based cognitive deficit does not ameliorate the pain-related cognitive impairment, although it may modulate or otherwise interact with it.

A second major concern is the need to extricate pain-related cognitive effects from those resulting from treatments for pain, especially from medications such as opioids that are well known to affect cognitive functioning.

A third complexity has to do with separating pain-related effects on cognition from the effects of the emotional distress that is a hallmark of chronic pain. The majority of pain patients suffer from depression, anxiety, stress, or a combination of these and related factors, all of which affect cognitive functioning directly or indirectly, via apathy, medication effects, fatigue, and disordered sleep.¹⁰ Notably, several studies that quantitated cognitive impairment found that such factors fully accounted for the observed numerical decrements.¹¹ Yet even in such studies, it is possible that cognitive impairments were initially the result of pain and only subsequently became statistically correlated with indices of depression.

A fourth concern is that symptom exaggerators up to and including frank malingerers may deliberately underperform on cognitive testing in the context of litigation and possible financial reward. Several studies have attempted to identify distorted scores by methodological means, such as by comparison with results of healthy individuals or chronic pain patients instructed explicitly to fake pain and behave so as to impress the tester that they are in pain, or by checking facial or muscular signs indicative of pain or its absence.¹²

A host of other issues render studies and conclusions in this domain complex. These include the need to interpret research findings in the context of factors such as age, previous testing (e.g., for intelligence level), and educational level of the participants. Additional factors applicable to all pain studies include pain duration, quality, mechanism, location, and comorbidity.¹³

The above complexities may tempt us to simply give up and wait until some future time when clear findings have emerged to support unequivocal conclusions about how chronic pain affects cognition. A more pragmatic approach would be to accept these difficulties and reason that if, despite the complexity and incompleteness of currently available evidence, some conclusions emerge, then "there must be something in them" that deserves consideration.

To identify these "somethings," we performed a systematic review of reports published since 1990 that evaluated the effects of chronic pain on cognitive processes. The review was based on checking the relevant publications that were found in PsychInfo and Medline in response to the search terms "pain" and "cognition"; the review has been submitted by the first author for publication. Studies were considered if they compared at least one measure of cognitive function in chronic pain patients and controls; included controls without acute or chronic pain; excluded patients whose chronic pain resulted from cancer, traumatic brain injury, or other neurological disorders; excluded those with primary major psychiatric disorders; and assessed cognitive functioning using valid and reliable tests. Of note, we did not exclude patients taking analgesic medications, because most patients with chronic pain use analgesics at some point. Further, we included findings about deficits in cognitive functioning that also correlated with indices of emotional distress, mainly depression. We did not wish to overlook or minimize the contribution of concurrent emotional factors such as depression or anxiety^{5,6} to cognitive deficits in chronic pain because the correlation with an emotional factor does not negate the existence of the cognitive deficit and does not indicate that chronic pain is not a causal factor for the deficit. Detailed information about our review is available from the first author (S.K.). What follows is a global summary of statistically significant findings in the 42 studies we retrieved, mostly of patients with chronic musculoskeletal pain (including whiplash injury) involving mixed sites.

A Starting Point: Patients' Complaints

In one comprehensive study, 54% of patients reported at least one problem with cognitive functioning, the most common problems being forgetfulness (23.4%), minor accidents (23.1%), difficulty finishing tasks (20.5%), and difficulty with attention (18.7%).³ In another study the most frequently reported memory complaints included problems when referring to films and books (61%), forgetfulness (44%), problems with handling of everyday tasks (38%) and with daily conversations (38%).¹⁴ In these and other studies, the subjective complaints were in part attributed to depression. In sum, such surveys identify problems with memory and attention as most prevalent in those with chronic pain.

Objective Findings

Memory deficits. Thirty of 34 publications that applied objective testing (88.2%) reported memory deficits; in these 30 studies, 63 memory measures or variables were used, of which 49 variables (77.8%) showed impairment by chronic pain. Not every measure was uniformly impaired across all studies; for example, the Trail Making Test yielded decreased results in five studies but no difference in two others. The memory assessments applied in these studies measured a varied set of functions, including verbal and nonverbal memory, immediate and delayed memory, and long-term and short-term memory, as well as memory span. On the whole, it seems justified to conclude that the most affected aspects of memory are those that involve delayed memory, rely heavily on verbal materials, and require new learning and retrieval of information previously acquired in the framework of newly learned tasks. There are

indications that memory for figural materials, visual memory, spatial memory, and incidental (nonintentional or spontaneous) memory are less affected by chronic pain. Two studies reported a bias toward worse recall by pain patients of pain-related words than neutral words.

Attention deficits. In 13 relevant publications, 9 studies (69.2%) showed attention deficits; in these studies, 16 attention measures were used, of which 9 measures (56.2%) showed lower performance during chronic pain. However, the attention measures on which pain patients did not differ from control participants without pain included some of the most firmly validated and most widely applied instruments in the field, namely, the Stroop interference task and the attention and concentration indices based on the Wechsler Memory Scale.

Verbal deficits. In 9 relevant publications, 8 (88.9%) reported deficits; in these studies 11 measures of verbal performance were used, out of which 9 measures (81.8%) showed lower scores for chronic pain patients. The applied measures included tests of vocabulary and tests of word or category fluency.

Speed deficits. In 17 relevant publications, 14 (82.3%) showed speed deficits; in these studies 32 speed measures were used, of which 23 measures (71.9%) had worse performance by chronic pain patients. The measures spanned varied aspects of speed, ranging from verbal tasks through information processing to psychomotor speed. The same measure sometimes showed a deficit in some studies, but not in others (such as the Paced Auditory Serial Addition Test, which showed decreased speed in only 8 of 11 studies). Notably, in all three applications of one speed test, the Number Connection Test, patients with chronic pain did not differ from healthy controls.

Mental flexibility deficits. Out of 11 relevant publications, 8 (72.7%) reported lower scores for chronic pain patients. In these studies 11 flexibility measures were used, based mostly on switching from one task or set of instructions to another; 8 measures (72.7%) showed lower performance by chronic pain patients.

Deficits in other cognitive functions. Reasoning was tested in four studies (in three of which pain patients scored lower); construction ability was tested in two studies (pain patients scored lower in both); calculation was tested in two studies (pain patients scored lower in both); and Block Design and Similarities were tested in two studies (in neither study did pain patients show a deficiency). Deficits in each of the following functions were reported in patients with chronic pain in one study: visual-motor coordination, abstract thinking, problem solving, and decision making in an emotional risk-involving task. In a gambling task based on a card game, the performance of chronic pain patients was poorer than that of healthy individuals; the net number of choices made from advantageous decks after subtracting choices made from disadvantageous decks was on the average lower in the chronic patient group than in the other group.

Overall measures of cognitive functioning. The three basic measures of overall cognitive functioning that have been used in studies of chronic pain are the Mini-Mental State Examination, the Neurobehavioral Cognitive Status Examination, and the Wechsler Adult Intelligence Scale (WAIS). These measures were applied in four studies. Two of these applied the WAIS: in one, but not the other, pain patients scored lower than controls.

On the Neurobehavioral Cognitive Status Examination test, 32% of the chronic pain patients had impaired performance. The score of chronic pain patients on the Mini-Mental State Examination was somewhat lower than of healthy individuals, but not significantly so.

Further Indications of Cognitive Impairment in Chronic Pain

The above-cited findings reflect comparisons of mean results from groups with and without chronic pain. Some researchers have in addition examined correlations between the degree of cognitive deficit and pain intensity. The validity of the latter approach is supported by the finding that cognitive impairment does not affect reported pain intensity.¹⁵ Pain intensity correlated positively with the number of subjective complaints of cognitive dysfunction (2 studies); with the degree of objectively assessed cognitive impairment in regard to mental flexibility (6 studies), memory (1 study), visual-motor coordination (1 study), speed (2 studies), and emotional risk-bound decision making (1 study); and with overall scores on the Repeatable Battery for Assessment of Neurological Status (1 study). However, no correlations were found between pain intensity and attention and concentration (1 study), memory (2 studies), word fluency (1 study), or speed assessed by a simple reaction time to presented stimuli (1 study).

Another strategy to explore the impact of pain on cognitive functioning is to assess the cognitive effects of pain reduction following successful treatment. While there is evidence for some improvement in auditory vigilance following reduction in pain intensity,¹⁶ another study found that significant reductions in pain intensity were accompanied by improvements in subjective evaluations of cognitive functioning but not in objective assessments of cognition.¹⁷

Both pain and cognitive functioning rely on brain activation. A review of studies in the 1990s provided clear evidence of abnormalities in regional cerebral blood flow during chronic pain.² Examining brain activation during pain provides another perspective on the problem at hand.^{18,19} One study successfully tested the hypothesis that delivering a painful stimulus such as thermal stimulation while participants are engaged in cognitive semantic tasks, such as category fluency and word repetition, would increase activation in brain regions engaged in the cognitive task, such as Broca's area. This study found that pain increased activity in brain areas directly involved in the cognitive task, as well as in other areas of the prefrontal cortex, and decreased activity in the perigenual cingulate cortex, insula, and medial thalamus.²⁰ Another study showed that pain-related brain activation in three cortical regions—the primary (S1) and secondary (S2) somatosensory cortices and the anterior insula—was attenuated by engagement in a cognitively demanding task, the Stroop test.²¹ Beyond suggesting a mechanism by which distraction can reduce pain intensity, findings of this kind also shed light on how cognitive performance may be impaired by pain. Human brain-imaging studies showing that brain regions critical for emotional decision making are also involved in chronic pain help account for the interesting discovery that pain impairs such decision-making tasks.²²

Early Conclusions

Our survey tentatively supports several conclusions in this important but still under-researched area. Most patients with chronic pain complain of cognitive difficulties, mainly with respect to memory and attention. Objective cognitive deficits are mainly in the domains of memory, attention, speed in performing structured tasks, speed in responding to stimuli of a cognitive task, verbal ability, and mental flexibility. The evidence concerning more complex cognitive functions is scarce, and the question remains open as to whether chronic pain affects these functions. In many cases the cognitive deficits may be at least partially explained by patients' depression and emotional distress. While these mood factors may account for cognitive difficulties, other explanations are possible, some of which have not yet been evaluated in depth. Some investigators argue for the attention overload explanation: if pain is considered as an attention-consuming stimulus and attention as a unitary and limited resource, subnormal attentional reserves may be left for cognitive functioning in chronic pain patients.^{23,24} Another possible explanation is that some patients with chronic pain have decreased motivation and interest in any activity, due to their persistent pain and associated anxiety or depression. Other plausible explanations are the effects of analgesics and fatigue caused by disordered sleep, as well as the above-noted impact of pain-induced brain activation in areas that mediate cognitive functioning.

Uncertainty as to the causes of these cognitive difficulties in no way exempts investigators and clinicians from taking them seriously. Investigators must address the spectrum of cognitive difficulties accompanying chronic pain and create methods to overcome them. Clinicians must recognize that examining cognitive functioning at multiple levels should be part of the assessment of every patient with chronic pain. This comprehensive clinical approach not only allows more precise tracking of the therapeutic outcomes, but also conforms with the modern view of pain as a multidimensional, biopsychosocial process whose optimal treatment considers the varied effects of this experience upon the entire person.

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This article, along with many other scholarly contributions, is published posthumously after Professor David Niv's recent tragic, untimely death. As one among many in David's worldwide circle of professional acquaintances who became personal friends, the Editor benefited along with many others from his energy, wide-ranging intellectual curiosity, and generosity of spirit. A tireless champion of the cause of pain relief, David played a seminal role in the founding of the European Federation of IASP Chapters, among numerous other pain-related initiatives and events worldwide. The Editor extends his condolences to the family and colleagues of this great man.

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