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The psychology of chronic post-surgical pain: new frontiers in risk factor identification, prevention and management

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Abstract

In an era of considerable advances in anaesthesiology and pain medicine, chronic pain after major surgery continues to be problematic. This article briefly reviews the known psychological risk and protective factors associated with the development of chronic postsurgical pain (CPSP). We begin with a definition of CPSP and then explain what we mean by a risk/protective factor. Next, we summarize known psychological risk and protective factors for CPSP. Psychological interventions that target risk factors and may impact postsurgical pain are reviewed, including the acceptance and commitment therapy (ACT)-based approach to CPSP prevention and management we use in the Transitional Pain Service (TPS) at the Toronto General Hospital. Finally, we conclude with recommendations for research in risk factor identification and psychological interventions to prevent CPSP. Several pre-surgical psychological risk factors for CPSP have been consistently identified in recent years. These include negative affective constructs, such as anxiety symptoms, depressive symptoms, pain catastrophizing and general psychological distress. In contrast, relatively few studies have examined psychological protective factors for CPSP. Psychological interventions that target known psychological risk factors while enhancing protective psychological factors may reduce new incidence of CPSP. The primary goal of our ACT intervention is to teach patients a mindful way of responding to their postsurgical pain that empowers them to interrupt the negative cycle of pain, distress, behavioural avoidance and escalating opioid use that can limit functioning and quality of life while paradoxically amplifying pain over time. Early clinical outcome data suggest that patients who receive care from TPS physicians reduce their pain and opioid use, yet patients who also receive our ACT intervention have a larger decrease in daily opioid dose while reporting less pain interference and lower depression scores.

Keywords

Chronic postsurgical pain, risk factors, protective factors, psychological interventions, acceptance and commitment therapy

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In an era of considerable advances in anaesthesiology and pain medicine, chronic pain after major surgery continues to be problematic. An early study on the prevalence of chronic postsurgical pain (CPSP) reported that 22.5% of 5130 chronic pain patients seen in 10 UK clinics indicated major surgery as its source.[1] Studies since then have specified that between 10% and 70% of major surgery patients go on to develop CPSP depending on the surgery type (e.g. cardiac, thoracic, gynaecological, spinal).[2,3] CPSP places considerable physical and psychological burdens on individuals initially hoping to improve or recover from medical conditions for which major surgery had been indicated. Given the proliferation of major, oftentimes necessary, surgeries for various medical illnesses over the years, there are potentially millions of individuals globally suffering from, and at risk for, CPSP on an annual basis. The burden of CPSP also falls under the purview of the opioid public health crisis.[4] Increasing numbers of chronic pain and major surgery patients remain on long-term, high-dose prescription opioids[5] with little to no medical assistance for tapering and incur risks for opioid dependence, misuse, addiction and even fatal overdoses.[4,5] The first step in addressing this pain, disability and suffering is to identify the causal, modifiable risk and protective factors that predict CPSP.

This article briefly reviews the known psychological risk and protective factors associated with the development of CPSP. We begin with a definition of CPSP and explain what we mean by a risk/protective factor. We then summarize known psychological risk and protective factors for CPSP. Psychological interventions that target risk factors and may impact postsurgical pain are reviewed, including the approach to CPSP prevention and management we use in the Transitional Pain Service (TPS) at the Toronto General Hospital. Finally, we conclude with recommendations for research in risk factor identification and psychological interventions to prevent CPSP.

Chronic postsurgical pain

Although there is considerable variability in surgical procedures and the time required to recover, the following 6-point definition appears to capture the most important aspects of CPSP.[6,7] The pain (1) developed after a surgical procedure, (2) is at least 2 months in duration, (3) interferes significantly with health-related quality of life, (4) is a continuation of acute postsurgical pain or develops after an asymptomatic period, (5) is localized to the surgical field and/or projected to territory or dermatome innervated by a nerve in the surgical field and (6) is not caused by other factors (e.g. pre-op pain, recurrence after surgery for cancer, chronic infection have been ruled out).

An understanding of the aetiology of CPSP begins with consideration of intraoperative factors, such as ongoing inflammatory processes arising from tissue damage, and neuropathic pain associated with intraoperative nerve damage, both of which may mark the beginning of the process by which acute time-limited pain transitions to chronic, pathological pain.[2,8–11] In addition, peripheral sensitization and central sensitization have been proposed as risk factors for the development of CPSP. Sensitization by way of injury discharge in the intraoperative and acute postoperative stages may cause neuroplastic changes resulting in the reduction in the threshold of nociceptor peripheral terminals (peripheral sensitization) or an increase in the excitability of brain and spinal cord neurons (central sensitization).[12–14] These changes contribute to the long-term amplification and maintenance of pain in individuals who develop CPSP and also help to explain the greater vulnerability of people who present for surgery with a pre-existing chronic pain condition.[2,3] The clinical presentation of CPSP likely involves a combination of the aforementioned mechanisms and other possibilities.[2] Further complicating the clinical picture are psychological factors, namely, perioperative depressive–anxiety symptoms and cognitive, emotional and traumatic reactions to pain that can modulate the experience of pain and play a contributing role in the manifestation of CPSP.[2,3,15]

Psychological risk and protective factors for CPSP

Risk/protective factor definition

A risk or protective factor is a measurable construct used to classify participants along a continuum of risk of the probability of developing an outcome of interest.[16] Risk/protective factors must be measured before the outcome has manifested. Participants are typically classified into a high-risk and a low-risk group using a common metric (e.g. odds ratio, relative risk ratio). Causal risk factors are distinguished from correlated risk factors on the basis of their likelihood to alter the outcome when modified. Modification of a causal risk factor reduces the risk of the outcome, whereas modification of a correlated risk factor has no effect on the outcome. In the case of CPSP, if intervening on a risk or protective factor prior to surgery, or in the acute post-surgical period, reduces the likelihood of transition to CPSP, then it can be considered a clinically important causal risk factor. The main aim of research on risk factor identification is to establish the causal, modifiable risk factors that confer a greater (or lesser) risk of developing CPSP. Identification of psychological risk and protective factors for CPSP is integral for the development and implementation of timely

psychological interventions to prevent and/or manage CPSP.

Psychological risk factors

Several pre-surgical psychological risk factors for CPSP have been consistently identified in recent years. These include negative affective constructs such as anxiety symptoms,[17–19] depressive symptoms,[20–22] pain catastrophizing[18,23,24] and general psychological distress.[25,26] Systematic reviews of psychosocial risk factors for CPSP indicate a high level of evidence (i.e. Grade of Association 1: Association Likely) for the predictive value of pre-surgical depression, psychological vulnerability and chronic stress on risk of persistent pain following surgery.[27] Pooled odds ratios (ORs) for pre-surgical anxiety (OR = 1.76, 95% confidence interval (CI): 1.07–2.90) and pre-surgical pain catastrophizing (OR = 2.37, 95% CI: 1.32–4.28) indicate that patients who present with these issues before surgery are approximately twice as likely to go on to develop CPSP compared with controls.[28] Newer constructs such as perceived injustice[24] and sensitivity to pain traumatization[29,30] also predict CPSP, but, with so few studies conducted to date, these findings require replication.

Psychological protective factors

Relatively few studies have examined psychological protective factors for CPSP. Psychological robustness, a composite variable comprising high dispositional optimism, high positive affect and low emotional distress, has been found to predict a lower incidence of CPSP at 4 months in women undergoing breast cancer surgery (OR = 0.70, 95% CI: 0.49–0.99).[31] In a study of patients undergoing coronary artery bypass graft, greater pre-operative optimism was found to be significantly associated with lower pain intensity and fewer physical symptoms following surgery, after controlling for demographic, clinical and behavioural covariates, including negative affectivity.[32] Both studies suggest that having an optimistic outlook with respect to outcomes of major surgery may help patients navigate their post-surgical recovery period. However, maintaining an optimistic outlook is not always possible when facing an uncertain future mired with health problems. Moreover, the recovery stage of major surgery oftentimes requires patients to endure significant pain, impairment and setbacks that can limit re-engagement with important daily activities. In this respect, protective factors pertaining to behavioural principles may lend more clarity to how patients may take an active role in their post-surgical recovery. Interestingly, a study has found lower pre-operative pain self-efficacy scores, which assess a person's confidence in performing general activities despite pain, to be a significant predictor of greater functional limitations, but not pain, at 1 year after total knee arthroplasty.[33] It is possible that pain self-efficacy assessed in the post-operative period would be an even stronger predictor of functional ability than pre-operative pain self-efficacy, due to the shift in expectations about function and perceived abilities one is likely to incur after undergoing a major operation. By contrast, another study has shown that patients with a higher pre-surgical score on the Patient Activation Measure (reflecting the propensity to engage in adaptive health behaviours) experienced better pain relief at 6 months after total knee arthroplasty.[34] Taken altogether, these studies indicate that fostering optimism and enhancing self-efficacy and adaptive behaviours in the perioperative period could improve outcomes for patients undergoing major surgeries.

Targeting psychological risk factors for CPSP using behavioural interventions

Psychological interventions that target known psychological risk factors while enhancing protective psychological factors may reduce new incidence of CPSP.[2] Psychological interventions for people living with chronic pain have a long track record of efficacy as part of multidisciplinary chronic pain treatment,[35,36] so it is reasonable to expect that the same tools and techniques could minimize acute post-operative pain intensity and improve quality of life by reducing distress, disability and chronic opioid use for patients who sustain neuropathic injury during surgery and are at risk for CPSP. Despite the long-standing evidence for psychological risk factors in CPSP, until quite recently there has been relatively little investigation into the efficacy of behavioural interventions aimed at targeting these risk factors perioperatively with the goal of preventing CPSP.

Behavioural interventions in the perioperative domain have largely targeted *acute* post-surgical outcomes such as pain intensity, anxiety, opioid use in the hours or days immediately after surgery and time to hospital discharge.[37] Pre-operative education (including information about the surgery, expected pain and pain medication, with content sometimes also addressing coping strategies) has long been known to reduce pre-surgical anxiety, leading to improved post-surgical outcomes, including reduced opioid consumption in hospital and shorter length of stay following surgery.[38–41] Relaxation, guided imagery and clinical hypnosis have been shown to reduce pain, use of analgesic medication and negative affect in the acute post-operative period.[37,42]

Cognitive-behavioural approaches common to chronic pain interventions have also been used with surgical patients. Scheel et al.[43] examined the impact of a brief cognitive-behavioural therapy (CBT) intervention for 48 young men undergoing surgical correction of a chest malformation. The intervention consisted of pain education, cognitive restructuring challenging pain catastrophizing, practice redirecting attention from pain to other sensory channels of perception and relaxation with a personalized audio recording. The intervention was delivered for 1 hour the day before surgery and for an additional hour 1–3 days after surgery. The intervention group reported lower acute pain intensity than the control group 1 week after surgery and less disability (but not significantly less pain intensity) 3 months later. At 6 and 12 months, there was no difference between groups in pain intensity or pain-related disability; however, at 12 months, when patients were anticipating a second surgery to remove the transsternal metal implant, a re-emergence of pain anxiety was found only in the control group, suggesting that the intervention group felt more empowered to deal with the pain of their upcoming surgery 1 year later.

CBT programmes can be combined with physical interventions for surgical patients, in the same way that CBT and physiotherapy are integrated in multidisciplinary chronic pain clinics. Archer et al.[44] randomized 86 patients undergoing laminectomy to either a cognitive-behavioural-based physical education programme (cognitive-behavioural play therapy) or an education programme at 6 weeks after surgery. At 3-month follow-up, play therapy participants had significantly greater decreases in pain and disability compared to the education group.

The TPS: targeting CPSP with acceptance and commitment therapy

In addition to controlled research trials, novel clinical initiatives have been developed to address psychological risk factors for CPSP. The innovative post-surgical TPS at Toronto General Hospital offers comprehensive, multidisciplinary pain management to patients at high risk of CPSP from pre-admission up to 6 months after surgery.[15] Clinical services include (1) multimodal medication optimization by anaesthesiologists, (2) post-surgical physiotherapy and (3) a pain psychology intervention consisting of pain education, mindfulness training and a form of cognitive-behavioural treatment called acceptance and commitment therapy (ACT).

ACT is part of a new wave of cognitive-behavioural approaches[45] that seamlessly integrates mindfulness.[46] ACT protocols have garnered substantial support as an intervention for chronic pain in a relatively short period of time.[47–49] In terms of CPSP risk factors, mindfulness and acceptance-based interventions have demonstrated efficacy in the treatment of depression and anxiety,[50–53] and although ACT does not target pain catastrophizing *per se*, mindfulness and acceptance-based interventions have been shown to lead to reduced pain catastrophizing.[54,55] Furthermore, brief ACT interventions for pain and other medical problems have been effective for, and acceptable to, medical patients.[56] ACT has shown promise in the treatment of opioid misuse, including higher rates of completed detoxification, reduced fear of detoxification and lower opiate and total drug use at follow-up than methadone alone or in combination with drug counselling.[57,58] There have been recent calls to expand the scope of ACT interventions to the treatment of post-surgical pain that may persist.[59]

In the TPS, the primary goal of the peri-surgical ACT intervention is to teach patients a mindful way of responding to their post-surgical pain that empowers them to interrupt the negative cycle of pain, distress, behavioural avoidance and escalating opioid use that can limit functioning and quality of life while paradoxically amplifying pain over time.[60] The overarching goal is to expand the post-surgical patient's capacity to experience pain – and the thoughts and feelings that come with pain – without rigidly engaging in problematic avoidance behaviour. Instead, pain sensations – as well as the mind's reactions to pain sensations – are observed neutrally and non-reactively, while motivation and commitment to engage in personally meaningful, goal-oriented activities are enhanced.[61] The end result is greater 'psychological flexibility', the ability to persist or adapt one's behaviour in the service of living a rich and purposeful life while in open psychological contact with internal experience, including pain. Our conceptualization of the six core ACT processes thought to underlie psychological flexibility and how they are at play in the post-surgical context can be seen in Figures 1 and 2. ACT clinicians use a variety of techniques to intervene on these six processes of change, including teaching metaphors, mindfulness practice and adaptations of familiar CBT tools such as exposure and behavioural activation.

Early clinical outcome data suggest that patients who receive care from TPS physicians reduce their pain and opioid use, yet patients who also receive our ACT intervention have a larger decrease in daily opioid dose while reporting less pain interference and lower depression scores.[62] In a preliminary, non-randomized study, 91 patients received ACT plus care from the TPS physicians, whereas 252 patients received care from only the TPS physicians. The following outcomes were compared between the two groups at the first and last TPS visits after surgery: pain intensity, pain interference,

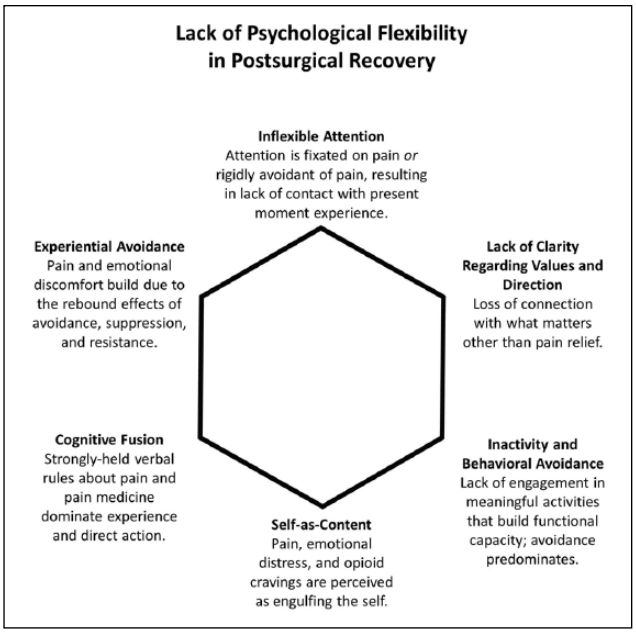

Figure 1. This clinical conceptualization of six psychological processes thought to underlie poor adjustment and recovery after surgery is based on the treatment model of acceptance and commitment therapy (ACT), as well as our clinical experience working with post-surgical patients in the Transitional Pain Service at Toronto General Hospital, a novel multidisciplinary pain service targeting the prevention and early comprehensive management of CPSP.

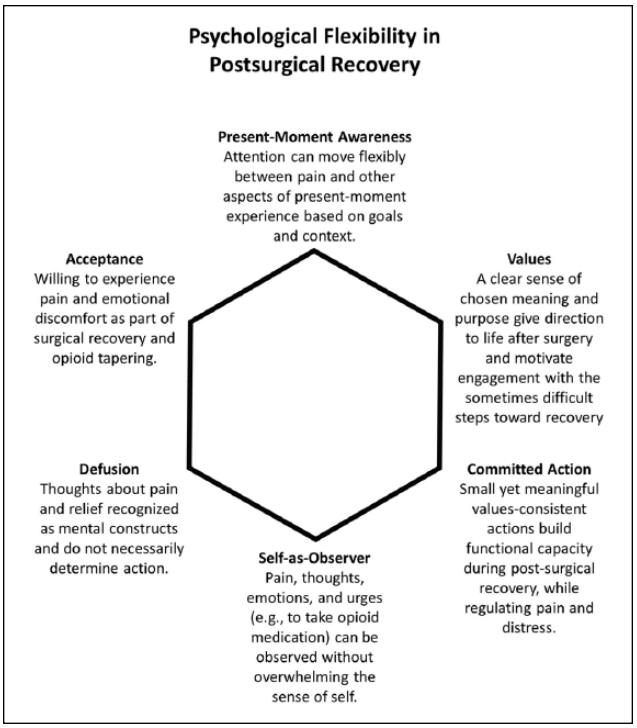

Figure 2. The Transitional Pain Service ACT intervention aims to develop these six facets of psychological flexibility in order to reduce distress, foster new skills for the self-management of pain (e.g. mindfulness skills), promote behavioural activation within functional limits and reduce psychological barriers to opioid weaning.

sensitivity to pain traumatization, pain catastrophizing, anxiety, depression and opioid use. The results showed that compared to patients who did not receive ACT, those who did were more likely to report a mental health condition pre-operatively, had higher opioid use at the first post-surgical visit, and also reported higher sensitivity to pain traumatization and higher anxiety scores at the first and last TPS visits. Despite these group differences, compared to the patients who did not receive ACT, those who did demonstrated greater reductions in opioid use and pain interference and showed reductions in depressed mood by the end of treatment.[62] These outcomes suggest ACT was effective in reducing opioid use while pain interference and mood improved, but they require replication in a randomized, controlled study.

Recommendations for future research

Risk/protective factor identification

Progress in risk factor identification research will be facilitated by attention to several interrelated methodological issues:

1. *Selection of risk factors*. Potential risk factors may be selected based on currently established risk factors for CPSP (e.g. depressive symptoms, anxiety), including those targeted by the leading, evidence-based behavioural pain management intervention for chronic pain, CBT (e.g. pain catastrophizing). Further investigation may gather evidentiary support for alternative models such as the ACT model, adding additional risk factors to the literature.[63] The identification of pre-operative risk factors that can be altered by clinical interventions is especially useful in the prevention of CPSP.
2. *Timing of risk factor assessment*. Ideally, risk factors should be assessed at least twice: once before and once after major surgery (e.g. in the days or weeks after). This will ensure that the issue of changing baselines does not confound assessment and lead to non-representative risk factor estimate.[64] Instances have been reported in which risk factors assessed pre-operatively do not predict CPSP, but assessment of the same factors assessed in the days or weeks after are predictive.[65] The same has been shown for early (days) and late (weeks) acute post-operative pain

intensity.[66] Timing of risk factor assessment is critical and may be surgery-specific.

3. *Timing of outcome assessment*. Studies rarely follow patients for more than a year after surgery and many assess CPSP only at 3 or 6 months when the pain has just transitioned to chronicity. Elsewhere, we have shown that the risk and protective factors involved in the transition of acute pain to chronic pain differ from the factors involved in maintaining the pain once it has become established.[66–68] The transition to CPSP and related psychosocial dysfunction is a dynamic process that evolves over time, necessitating outcome assessment at more than one point after surgery. Assessing outcomes at a single point in time after surgery will not permit an examination of whether the factors involved in the transition to chronicity differ from those involved in the maintenance of already established chronic pain. Moreover, modifying a time-dependent, causal risk factor that predicts CPSP early after surgery (e.g. 3 months), but not later on (e.g. 1 year), will have no effect on the later outcome.
4. *Patient-centred data analysis*. The traditional approach to studying CPSP has involved a single measure (e.g. pre-operative anxiety) or an average of several measurements across the perioperative period as predictors of CPSP. Examination of patient trajectories after major surgery is an emerging, novel approach to studying the dynamic, evolving nature of the development and maintenance of CPSP. Use of latent trajectories allows for the clustering of patient subgroups that share similar trajectory characteristics and therefore take into account the heterogeneity of psychological experiences over time.[69,70] Trajectory-based analyses of post-surgical pain may help identify patients in need of post-surgical intervention, such as those with consistent levels of acute post-operative pain and elevated anxiety symptoms.

Intervention research

Substantial research is needed to establish how psychological and behavioural interventions can be maximally effective in addressing psychological risk factors for CPSP:

1. *Research on behavioural treatment modalities*. Research is needed on a range of intervention options, including psycho-education, hypnosis, CBT, mindfulness and ACT. These psychological interventions could be offered separately or in treatment packages where they are combined with one another or with other interventions such as physiotherapy.
2. *How much behavioural treatment is needed and when can it help the most?* The timing (pre-surgical, acute post-surgical and/or long-term 'booster sessions') and 'dosing' of the amount of behavioural treatment needed are not yet understood (i.e. number of hours of contact with behavioural clinician, as well as 'homework' practice including relaxation, mindfulness and/or self-hypnosis).
3. *Measuring risk factors and key outcomes longitudinally*. Controlled intervention trials are needed that prospectively and longitudinally track key psychological risk factors (anxiety, depression, pain catastrophizing or other constructs associated with poor pain coping, and substance misuse history) and clinical outcomes (such as pain, disability, mood and opioid use) at key time points up to a minimum of 1 year after major surgery. Extending outcome assessment to 5 years after surgery would provide a much clearer idea of the natural course of CPSP.
4. *Assessing interventions across a wide range of surgeries*. There is great diversity in the surgeries that are conducted and in their long-term impact. Research should be conducted across a range of surgeries, including surgeries understood to confer greater risk of CPSP due to high risk of nerve injury (e.g. thoracic surgery, breast cancer surgery and amputations).[9–11,71]
5. *Targeting subgroups of patients*. Interventions may be developed to specifically meet the needs of specific subtypes of patients, such as those with a history of chronic pain or those with a history of substance misuse.

From risk factors to effective interventions

It is time to translate our growing understanding of the psychological risk factors predictive of CPSP into effective psychological interventions that improve patient quality of life. In 2017, the International Association for the Study of Pain's (IASP) Global Year Against Pain After Surgery, we have the tools that we need to move forward: awareness of key psychological risk factors for CPSP; effective psychological interventions for acute post-surgical pain, including education and hypnosis;[37,42] and a large body of research on the efficacy of CBT, mindfulness training and ACT for a variety of chronic pain conditions.[36,48] The time is ripe for a leap forward in experimental investigations as well as clinical care for the millions of people each year

who undergo necessary, often live-saving surgeries and are surprised to find their recovery marred by unexpected and debilitating long-term pain.

Conflict of interest

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