# INVESTIGATING THE ROLE OF AUTOBIOGRAPHICAL MEMORY IN POSTSURGICAL PAIN UP TO 1 YEAR AFTER MAJOR SURGERY

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## Abstract

Recent cross-sectional studies have identified differences in autobiographical memory among individuals with chronic pain, but the temporal relationship between the two is unknown. Moreover, autobiographical memory has yet to be studied in patients undergoing major surgery. This project addressed these gaps by conducting a prospective, longitudinal study of memory performance, postsurgical pain, and psychosocial factors in 97 adult participants scheduled for major surgery. Memories were evaluated using the Autobiographical Memory Test before and one month after surgery when participants were asked to recall personal events related to positive and pain-related word cues. Responses were coded for level of specificity, emotional valence, and surgery-related content. Questionnaires assessing presence/absence of pain and psychological functioning were administered before and at 1-, 3-, 6-, and 12-month follow-ups. Generalized estimating equations modelled pain at each postsurgical timepoint with memory variables as predictors. As hypothesized, higher numbers of specific pain memories recalled before surgery predicted lower odds of pain across all timepoints (OR=0.58, 95% CI [0.37-0.91]). Participants who took longer to recall pain memories before surgery (OR=2.65, 95% CI [1.31-5.37])) and those who produced more surgery-related content at the one-month assessment (OR=1.31, 95% CI [1.02-1.68]) had greater odds of reporting postsurgical pain up to 12 months later. These findings indicate that pre-surgical autobiographical memory biases are risk factors for development and maintenance of postsurgical pain. To the extent that these biases are causal, presurgical interventions that modify the quality and content of patients' memories may prove to be promising strategies in the prevention of chronic postsurgical pain.


*Keywords:* chronic pain, autobiographical memory, major surgery, chronic postsurgical pain

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## Published Material

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Some of the ideas and material contained in the Introduction and General Discussion of this thesis derive from Waisman, A., Pavlova, M., Noel, M., & Katz, J. (2022). Painful reminders: Involvement of the autobiographical memory system in pediatric postsurgical pain and the transition to chronicity. *Canadian Journal of Pain*, *6*(2), 121–141. https://doi.org/10.1080/24740527.2022.2058474. This is an open access article distributed under the terms of the Creative Commons CC BY license, which permits unrestricted use, distribution, reproduction in any medium, provided the original work is properly cited.

## Introduction

Chronic postsurgical pain (CPSP) is a surgical complication characterized by pain that persists beyond normal healing time (Schug et al., 2019). CPSP occurs in 10 to 70% of patients depending on the surgical procedure (Fletcher et al., 2015; Glare et al., 2019; Katz & Seltzer, 2009) and is responsible for approximately 25% of referrals to chronic pain clinics (Crombie et al., 1998). The need to prevent and effectively manage CPSP is critical given its alarming prevalence worldwide and its incidence, which adds millions of new cases to the roster each year (Katz & Seltzer, 2009; Meara et al., 2016). Identifying causal, modifiable risk and protective factors for CPSP can facilitate this goal and advance our overall understanding of the transition from acute to chronic pain (Katz & Seltzer, 2009; Price et al., 2018).

In addition to its debilitating physical sequelae, chronic pain is associated with alterations in memory, especially for pain (Larbig et al., 2019; Noel et al., 2017; Noel et al., 2015). One area that warrants attention for its potential role in initiating and maintaining chronic pain is autobiographical memory. Autobiographical memory refers to a system of memories for one's personal past consisting of episodic and semantic components. The coherent and flexible construction of these memories is integral to one's sense of self-continuity (Habermas & Kober, 2015; Tippett et al., 2018) and well-being (Conway et al., 2004; Fivush, 2011), facilitating everyday behaviours such as planning and imagining the future (Addis & Schacter, 2011; Addis et al., 2007), problem-solving (Sheldon et al., 2015; Sutherland & Bryant, 2008), and emotional regulation (Raes et al., 2003). A phenomenon known as overgeneral autobiographical memory (OGM) describes a tendency to recollect personal memories that lack temporal specificity (Williams & Broadbent, 1986). Whereas an overgeneral bias is well-established in mood disorders (Ono et al., 2016; Williams et al., 2007), relatively little is known about autobiographical memory in chronic pain.

Several studies have found greater overgenerality or reduced specificity (Liu et al., 2014; Quenstedt et al., 2020; Vucurovic et al., 2019) and differences in retrieval latency among individuals with chronic pain compared to pain-free controls (Liu et al., 2014; Wright & Morley, 1995). Individuals with chronic pain have also been found to generate more pain-related and emotional differences in the content of their recollections and imagined future episodes (Meyer et al., 2015; Quenstedt et al., 2020; Siqveland et al., 2019; Wright & Morley, 1995). However, since not a single prospective study has evaluated memory specificity and its association with pain, the temporal relationship between the two remains unknown and hypotheses about determinant factors cannot be ruled out. Moreover, to our knowledge, memory specificity and its relation to pain has yet to be examined in individuals undergoing major surgery. This project sought to address these gaps.

**Defining Pain**

In 2020, the International Association for the Study of Pain (IASP) revised the definition of pain to: "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (Raja et al., 2020). *Chronic pain* is generally recognized as having a duration of more than three months (Treede et al., 2019). It is classified as either *chronic primary pain* which refers to pain that that is considered to be a disease or a disorder in its own right and cannot be better accounted for by other chronic pain conditions or *chronic secondary pain,* in which case pain is regarded as a symptom of an another underlying disorder (Treede et al., 2019). Chronic pain is estimated to affect about 20% of the population worldwide (Goldberg & McGee, 2011), equivalent to approximately 7.6 million Canadians

(Health Canada, 2019). A leading cause of this suffering is a type of chronic secondary pain known as *chronic postsurgical pain* (CPSP). CPSP is an unanticipated surgical complication responsible for approximately 25% of referrals to chronic pain clinics (Crombie et al., 1998). Whereas the vast majority of individuals recover without sequelae, upwards of 70% of patients (depending on the surgical procedure) develop CPSP (Fletcher et al., 2015; Glare et al., 2019; Katz & Seltzer, 2009).

CPSP is defined by the following criteria: 1) the pain develops or increases in intensity after the surgical procedure, 2) the pain persists beyond normal healing time (typically at least 3-6 months), 3) the pain is localized to the surgical field, 4) the pain is not caused by other factors (e.g., pre-existing pain, infection, cancer recurrence), 5) the possibility that the pain is continuing from a pre-existing problem should be excluded when possible, and 6) the pain interferes significantly with one's quality of life (Macrae, 2008; Macrae & Davies, 1999; Werner & Kongsgaard, 2014). With tens of millions of individuals undergoing major surgery in the U.S. each year (Hall et al., 2010) or hundreds of millions worldwide, the one-year incidence of moderate to severe CPSP is about 5-10% (Fletcher et al., 2015; Weiser et al., 2015). This figure is variable and depends on many factors including the type of surgery in which case the incidence can range from ~10% for a less invasive surgery such as dental or hernia repair to as high as 30-85% for limb amputation (Schug & Bruce, 2017). CPSP is not only the source of immense suffering, but also presents a substantial economic burden, considering that the national annual cost of new cases of CPSP in Canada is estimated to be millions of dollars (Huang et al., 2016). The need to prevent and effectively manage CPSP is critical. Identifying causal, modifiable risk and protective factors can facilitate this goal (Price et al., 2018) and furthermore, research on the development of CPSP can advance our overall understanding of the transition from acute to chronic pain by serving as a useful general model for studying how, why, and in whom pain becomes chronic regardless of the inciting event (Katz & Seltzer, 2009; Price et al., 2018).

**Defining Risk Factors**

Risk is defined as the probability of an outcome in a given population (Kraemer et al., 1997). A *risk factor* is a characteristic that precedes the outcome of interest before it develops and is associated with a greater likelihood of negative outcomes (Kraemer et al., 1997). Protective factors are defined in the same way except they are associated with a lower likelihood of negative outcomes and might act to reduce a risk factor's impact. In the case of CPSP, a risk factor must be measured either before surgery or after surgery but before chronic pain develops. Variables measured concurrently or after the fact, for example in the form of a symptom, are known as *correlated factors* (Kraemer et al., 1997). For this reason, prospective longitudinal designs are necessary for identifying predictive factors as they allow for participants to be followed across time from before to after a given outcome occurs.

Risk factors can be either *fixed/non-modifiable* referring to innate characteristics that are not subject to change or *variable/modifiable*. The latter can be manipulated to determine whether it changes the outcome. If it does, then this would signify the presence of a *causal risk factor*. Causal risk factors can be identified through randomized controlled trials and are of most interest to researchers because this informs the development of interventions that have the potential to reduce the risk of chronic pain before it develops. By contrast, if manipulating a modifiable risk factor does not alter the outcome of interest, then it is considered a *correlated risk factor*. Thus, intervening on non-causal risk factors is futile given that this would not mitigate the probability of a negative outcome (Katz et al., 2011; Katz et al., 2022).

An important point that has been previously noted in this line of research is the distinction between predictive factors involved in the *transition* to chronicity and those involved in the *maintenance* of already established chronic pain (Katz, 2012). Risk factors identified before surgery or in the acute stage afterward predict the transition to chronic pain, whereas factors assessed once pain has already become chronic in the months (e.g., at three or six months) following surgery predict its maintenance. For example, a prospective longitudinal study conducted by Katz et al. (2009) examined individuals after lateral thoracotomy and found that preoperative pain disability and emotional numbing as well as pain intensity assessed in the acute postoperative stage did not significantly predict pain disability 6 or 12 months after surgery, or in other words, the *transition* to pain chronicity. However, when assessed at the 6 months follow-up, the same variables were found to be predictors of pain disability reported 12 months after surgery, reflecting the *maintenance* of chronic pain. A similar pattern can be observed in a study by Seebach et al. (2012) where several positive and negative affect variables failed to predict various pain-related outcome variables assessed 6 weeks and 3 months after surgery, but did predict some of those same variables at 3-months when the predictors were assessed at 6-weeks.

As pointed out by Katz (2012) the results of these studies provide examples of how the transition to CPSP is a dynamic process that evolves over time. Consequently, it is important to examine factors that predict the transition to chronicity independently from those that predict its persistence, considering that different mechanisms and risk factors might be involved at each stage. Furthermore, these findings underscore the importance of assessing outcomes at more than one time point before, during, and after surgery. These findings point to important considerations for conducting research on risk factors associated with surgery (Katz, 2012).

## Domains of Risk Factors for CPSP

Risk factors for CPSP have been identified at each stage of the perioperative trajectory including before, during, and after surgery (Katz & Seltzer, 2009; Schug & Bruce, 2017; VanDenKerkhof et al., 2012). The point at which one intervenes along the surgical trajectory is important because it corresponds to different levels of prevention. That is, depending on when intervention is implemented, treatment efforts can either prevent acute pain from occurring or becoming chronic, prevent chronic pain from becoming more severe, or manage chronic pain and its sequalae after they develop. Research into risk factors from the presurgical stage is important because elucidating this enables clinicians to recognize individuals who are at greater risk prior to the pain-eliciting event and implement preventative or early interventions that reduce the likelihood of CPSP, which in most cases, is more effective than retroactively treating pain after it has become chronic (Rosenbloom et al., 2021).

In addition to temporal stratification, CPSP risk factors can also be categorized according to the following broad domains: surgical, genetic, demographic, clinical, pain, and psychosocial factors (Katz & Seltzer, 2009; Schug & Bruce, 2017). There is some variation in how some sources group these risk factors with some for example including patient-related, anesthetic/analgesic, social environmental, psychological-emotional, and cognitive-neuropsychological categories as well as (Katz & Seltzer, 2009). Nonetheless, differences between the varying standards of categorization are subtle and largely overlap in the content that they capture. The following subsections do not cover all the risk factor domains previously mentioned; only the ones that are pertinent to this project will be described.

### *Surgical Risk Factors*

The type of surgery one undergoes is known to be a major risk factor for CPSP and as previously mentioned, corresponds to different incidence rates. Although not all CPSP is neuropathic, surgeries that involve damage to nerves lead to the highest prevalence (Hayes et al., 2002; Katz & Seltzer, 2009; Liem et al., 2003). Indeed, intraoperative nerve damage is thought to be the main underlying culprit responsible for both acute and chronic postsurgical pain (Katz & Seltzer, 2009). Other surgical risk factors include increased procedural duration (Kalso et al., 2001; Peters et al., 2007), low volume surgical units (Tasmuth et al., 1999), open as opposed to laparoscopic surgical approach (Liem et al., 2003), and peri- as opposed to intracostal suturing (Cerfolio et al., 2003).

### *Demographic Risk Factors*

Within the demographic domain, age is one of the most consistent risk factors for CPSP identified in most studies across a variety of surgeries, where those who go on to develop CPSP are found to be significantly younger than those who do not (Kalkman et al., 2003; Poleshuck et al., 2006). Interestingly, this trend contrasts that established in other chronic pain conditions in which increased age has been found to predispose individuals to higher rates of chronic pain (Dahlhamer et al., 2018; Tsang et al., 2008). This pattern does not however extend to very young age or pediatric age groups. Female gender which is a known risk factor for more severe acute (Schnabel et al., 2020) and more common chronic pain states (Tsang et al., 2008), is also often linked to CPSP (Kalkman et al., 2003), although not universally across all studies (Aternali et al., 2022). Other demographic factors are less reliably observed but include clinical risk factors such as overall health and medical comorbidity (VanDenKerkhof et al., 2012).

### *Pain-related Risk Factors*

The most robust predictor of CPSP is pain itself (Correll, 2017; Forsythe et al., 2008; Kalso et al., 2001; Katz & Seltzer, 2009; Pinto et al., 2013). This includes pain from all perioperative timepoints (Schug & Bruce, 2017). The presence, intensity, and duration of preoperative pain is a risk factor for both severe acute postoperative pain and chronic postsurgical pain (Katz & Seltzer, 2009; VanDenKerkhof et al., 2013). As well, pain affecting other parts of the body not necessarily localized to the surgical field increases risk of CPSP (Katz & Seltzer, 2009; VanDenKerkhof et al., 2013). Furthermore, the severity of acute postoperative pain in the days and weeks following surgery predicts pain after discharge and the development of CPSP (Katz & Seltzer, 2009). For example, it has been reported that for every 10% increase in the duration spent under severe pain during the initial 24 hours after surgery, the risk of developing CPSP increased by 30% (Correll, 2017). A potential explanation for this might be that acute postoperative pain is a sign of heightened pain susceptibility or a consequence of poor postoperative pain management (Katz & Seltzer, 2009). If this is the case, then managing this pain could reduce the chances of having poorer pain outcomes later on. However, rather than being a predictive factor, severe acute postsurgical pain has also been proposed to be an early manifestation of CPSP (Gerbershagen, 2013; Schug & Bruce, 2017), which if true, might challenge criteria 4 and 5 for the diagnosis of CPSP which state that the possibility of chronic pain being caused by or persisting from pre-existing pain must be ruled out. Other proposed explanations for why pain might be a predictor of subsequent pain include intraoperative nerve damage, unidentified pain genes, central sensitization induced by surgery and maintained by peripheral input, structural changes in the central nervous system induced by perioperative nociceptive activity, response biases, social environmental factors such as solicitous responding from significant others and social support that can unintentionally negatively reinforce an individual's pain behaviours, publication bias for significant findings, and psychological and emotional factors that contribute to pre-existing pain which are also related to postoperative pain (Katz & Seltzer, 2009). Finally, higher consumption of both pre- and postoperative analgesics, a proxy for intense pain, is associated with the development of more intense CPSP (Huang et al., 2016).

### ***Psychological and Emotional Risk Factors***

There are various psychological and emotional risk factors that have been identified for CPSP (Hinrichs-Rocker et al., 2009; Theunissen et al., 2012). These include depressive symptoms (Attal et al., 2014); state and trait anxiety (Choinière et al., 2014; Judge et al., 2012; Theunissen et al., 2012); fear of pain and surgery (Peters et al., 2007); general psychological distress encompassing general symptoms of stress, anxiety, and depression (Lingard & Riddle, 2007; Mejdahl et al., 2015); and introverted personality (Borly et al., 1999). Perioperative pain catastrophizing which refers to magnification, rumination, and helplessness related to pain has in some cases been found to predict postsurgical outcomes such as duration and intensity of pain in adults (Forsythe et al., 2008; Masselin-Dubois et al., 2013; Riddle et al., 2010), although this pattern is not ubiquitous across all studies (Aternali et al., 2022). Other more recently identified factors include sensitivity to pain traumatization defined as the propensity to develop anxiety-related responses to pain that resemble a traumatic stress response (Kleiman et al., 2011), as well as distress about bodily sensations which has been found to predict pain intensity and disability 6 months after cardiothoracic surgery (Aternali et al., 2022). Nonetheless, research on the psychological risk factors for CPSP remains largely uncharted. One such area that has recently been identified for its involvement in chronic pain is autobiographical memory, especially for pain (Larbig et al., 2019; Noel et al., 2017; Noel et al., 2019). Investigating memory for pain is important for several reasons. First, patients' recall of their pain experiences is a necessary component of assessment and diagnosis. Understanding the various biases that might exist in individuals' memory can help improve clinical interpretations of patients' self-reports (Erskine et al., 1990). Furthermore, elucidating the factors involved in initiating and maintaining pain after surgery can inform pain prevention and treatment strategies to stop pain before it becomes chronic.

**Defining Pain Memory**

The term "pain memory" has been used to refer to various phenomena in the field of pain. First introduced by Dennis and Melzack (1979) to explain the persistence of pain behaviours in a rodent model of deafferentation, it was later used in a human context by Katz and Melzack (1990), to describe phantom limb sensations and pains in limb amputees that closely resembled those that they had experienced in the limb before amputation and that persisted despite removal of the affected limb. The authors distinguished between two memory components underlying these experiences: The "somatosensory" component, which referred to unconscious, non-declarative/implicit memories and the "cognitive" component pertaining to declarative/explicit memories characterized by conscious retrieval processes responsible for contextualizing painful experiences, sometimes through recollections of specific events. Since its introduction thirty-one years ago, investigation into the latter has led to the discovery that certain aspects of declarative memory are in fact distorted in chronic pain (Redelmeier et al., 2003), often with compromising implications for postsurgical pain outcomes particularly identified in the pediatric literature (Noel et al., 2012; Noel et al., 2017). As such, it is unsurprising that a growing area in the field of chronic pain has focused on the study of various types of memory biases and their effects on individuals' pain trajectories. The term "pain memory" has been used in different contexts to refer to patents' declarative memories of the intensity, distress, and sensory quality of their pain experiences (Morley, 1993; Noel et al., 2012; Noel et al., 2017; Noel et al., 2019).

**Assessments of Memory for Pain**

Until recently, much of the research on memory for pain has focused on investigating the accuracy of individuals' recollections about painful experiences based on single item, self-report pain measures such as a 0-10 numeric pain rating scale (NRS) or 10 cm visual analogue scale (VAS) for pain intensity and pain affect or anxiety. One approach has been to calculate the difference between an individual's recall of pain intensity and the initial pain score obtained when they were in pain (Chen et al., 2000). Higher difference scores are taken as an indication of an "exaggeration in negative memory" in which the memory of pain is greater than initial pain. Others use the terms "negatively-biased pain memory" when the NRS score for recalled pain is higher than the initial pain score and "positively-biased pain memory" when the initial NRS pain score is higher than the recall score (Noel et al., 2019). Significant correlations between the numerical ratings for the actual pain experience and recollected pain have been interpreted to indicate accuracy of recall (Erskine et al., 1990). However, it is important to note that correlations indicate the degree to which values from the two timepoints change together, which can occur without necessarily having any overlap in the two distributions.

Regarding memory recall in surgical patients, in pediatric populations, studies have found that remembering painful events in a negative way is associated with worse postsurgical pain outcomes where children's memory for postsurgical pain intensity has been found to be a stronger predictor of reported pain levels five months after the surgery than the initial pain ratings (Noel et al., 2017). Furthermore, in a prospective longitudinal study of 237 children who underwent various surgical procedures, Noel et al. (2019) demonstrated that children who developed negatively-biased memories for pain intensity one year after surgery had more intense pain at the 6- and 12-month follow-up than those with accurate or positive memories. Psychological factors played an important role in this relationship where higher levels of baseline anxiety sensitivity and pain catastrophizing in the days after surgery while in hospital (i.e., 48 to 72 hours), predicted adolescents' negatively biased memories at the 12-month follow-up. Parallel findings are evident in a previous study where parental anxiety and higher levels of postsurgical pain predicted negatively-biased pain memories in young children undergoing tonsillectomy. Similarly, child and parent pain catastrophizing have also been shown to be associated with biased pain memory development in adolescents undergoing spinal fusion and pectus repair (Noel et al., 2015). Although these findings highlight the importance of memory biases in surgical patients' pain outcomes, this method of assessing pain memories is limited in that it reduces memory for pain intensity or pain affect to a deviation from the original score or to a partial correlation coefficient controlling for initial pain measured using a simple single-item NRS or VAS. A widely overlooked area in the study of pain, has to do with the episodic quality of the autobiographical memories themselves as generated by narrative descriptions.

It has previously been stated that memory for the sensory quality of a painful episode is impossible to vividly recall and as a result, very difficult to study (Jones, 1957). Attempts to assess the "quality" of one's pain recall have included comparing participants' responses on subscales of the McGill Pain Questionnaire (MPQ) to determine the accuracy of the memory quality. Typically, accuracy has been measured through various methods including comparing the most frequently selected pain descriptors from the MPQ (Brodie & Niven, 2000; Roche & Gijsbers, 1986) or by evaluating reliability coefficients between timepoints (Brodie & Niven, 2000). Findings on these comparisons yield mixed results, with some indicating that recall for the quality of one's pain is better than its intensity among adults undergoing surgery (Roche & Gijsbers, 1986), whereas others have found it to be generally poor or fair at best (Beese & Morley, 1993; Niven & Brodie, 1996). However, as pointed out by Erskine et al. (1990), studies that rely on subjects' verbal descriptions of their pain and subsequent recall might not be entirely valid since they might be measuring memory for words rather than memory for pain.

Another issue that has been raised with the method of retrospectively recalling ratings for pain-related experiences is that these recollections might not reflect episodic autobiographical memories for one's pain, but rather descriptions of semantic knowledge about a given pain in general (Brodie & Niven, 2000; Niven & Brodie, 1996). One study investigating the quality of individuals' recall for labour pain showed that women who had given birth were no more accurate at recalling ratings they made regarding the quality of their pain as assessed by the MPQ 3-4 years later than women who had never given birth (Niven & Brodie, 1996). This aligns with findings from another study in which two groups of menstruating women consisting of those who had and those had not experienced period pains before were asked to assess the severity and quality of period pain (either based on their own experience or inferences about what the pain might be like, depending on which group they belonged to), and then recall their ratings two weeks later (Brodie & Niven, 2000). The study found that women who had never experienced menstrual pain tended to overestimate ratings pertaining to pain severity but had comparable recall for ratings of pain quality on the MPQ relative to those who had experienced period pains. Based on these results, it has been proposed that episodic memory minimally contributes to recalling the qualitative aspects of pain whereas semantic memory allows for those who do and do not experience a given pain to similarly estimate its core qualities (Brodie & Niven, 2000).

Others have also emphasized a distinction between acute and chronic pain, proposing that acute pain is associated with more accurate recall for pain intensity than pain that is chronic or repeated (Erskine et al., 1990). They attribute this to the fact that in chronic pain, individuals are more likely to be influenced by a constant and pervasive conceptualization of their pain which draws on semantic memory rather than the severity or quality of the pain which would be at the forefront when recalling a specific pain event which taps episodic memory.

Terry et al. (2008) corroborated some of these findings in surgical patients. The authors assessed whether intensity and quality pain ratings made postoperatively by patients undergoing vascular surgery were comparable to estimates provided by nonpatients who did not undergo surgery but received informational pamphlets about the procedure. The study consisted of three groups consisting of patients who underwent vascular surgery and provided ratings immediately after and 4-6 weeks later, nonpatients who read a comprehensive, detailed informational pamphlet about the procedure and were asked to report pain estimates 4-6 weeks apart, and nonpatients who read a general pamphlet about the procedure and were also asked to provide estimates 4-6 weeks apart. Similar to previous findings, the results showed that nonpatients overestimated numerical ratings of pain severity and that both nonpatient groups used qualitative descriptors of pain comparable to patients. Although pain ratings did not significantly differ between those who did and did not experience a given pain, the authors noted that this does not necessarily imply that pain cannot be remembered. They suggested that to clarify this issue, studies should more explicitly investigate whether the recollections individuals provide regarding pain are for an actual experience or what they assume the pain should be like. In accordance with this, an earlier study by Terry et al. (2007) administered a remember/know paradigm to assess whether acute pain is remembered or known in the form of an autobiographical semantic memory. Participants were asked to rate their acute pain on the MPQ and VAS in anticipation of and immediate after undergoing a cold pressor task. They then provided ratings 2 weeks later at which point they also indicated whether each retrospectively reported MPQ descriptor of their pain experience was something that they remembered or knew. The results showed that anticipated ratings significantly underestimated the intensity of actual pain, whereas retrospective ratings did not differ from actual pain. More descriptors for the quality of pain were recalled as "remembered" and a greater proportion of remember judgments were more accurate than those deemed "known". The authors concluded that the remember/know paradigm allowed for a better assessment of one's true memory for pain than other traditional methods and stated that using this sort of paradigm could elucidate our understanding of the phenomenological experience of recalling past pain-related episodes.

Evidently, the need to investigate the phenomenology of memory for pain is a long-standing issue that has been extensively discussed throughout the literature for decades. In their 1990 review, Erskine et al. stated that "…we know almost nothing about the ability to remember the different components of pain: its intensity, sensory quality, affective tone and associated cognitive and behavioural activities" (p. 256). Yet, while the approach of assessing memory by comparing responses on single-item pain measures administered at the time of the inciting painful event and again at the time of recall taps some of the memory's sensory and affective components, it does not quite address the true phenomenological qualities or ability to re-experience a painful event. It is only very recently that a small subset of studies have begun to investigate these characteristics such as spatiotemporal specificity that is so integral to autobiographical memory.

**Autobiographical Memory**

Autobiographical memory refers to a declarative memory system comprised of specific past events known as episodic memory and general semantic knowledge about oneself and the world known as semantic memory (Tulving, 1972). These two components are highly interdependent and often influence each other at various stages of memory processing (Greenberg & Verfaellie, 2010; Svoboda et al., 2006). Autobiographical memory is necessary for our ability to perform various fundamental, non-mnemonic functions such as directing future behaviour through imagination, problem-solving, and decision-making (Addis et al., 2007; Jing et al., 2016; Pillemer et al., 2003; Schacter & Addis, 2007; Sheldon et al., 2015). It allows us to maintain a positive self-image (Wilson & Ross, 2001) and sense of self-continuity over time (Bluck & Alea, 2008; Conway, 2005), foster and sustain social relationships with others (Alea & Bluck, 2003, 2007), regulate negative emotionality (Jing et al., 2016; Williams et al., 2007), think creatively (Madore et al., 2015; Roberts & Addis, 2018), and solve problems efficiently (Peters et al., 2019).

The episodic component of autobiographical memory is defined by autonoetic consciousness which is the ability to mentally project oneself across time to ‘re-experience’ specific events from the past and to imagine the future (Tulving, 2002). Rather than being reconstructed replicas of prior experiences, episodic memories entail constructive processes that are prone to error (Bartlett, 1932; Bernstein & Loftus, 2009; Loftus et al., 1978; Schacter, 1996). That is, episodic memory is considered to be the product of binding accurate event details with relevant semantic or schematic knowledge and details from other events in order to fill gaps in remembering and make memories more coherent (Alba & Hasher, 1983; Bartlett, 1932). Therefore, the way that people remember and interpret their life experiences, to a great extent, depends on pre-existing knowledge and preconceptions about the world (Bernstein & Loftus, 2009). On one hand, prior knowledge can enhance new memories by integrating episodes within an existing semantic network (Bransford & Johnson, 1972; Craik & Tulving, 1975). Conversely, semantic elaboration processes at encoding can also lead to biases that result in memory distortions (Schacter et al., 2011). While these flaws in memory might appear fundamentally disadvantageous, a memory system that is constructive in nature serves an adaptive role as it allows individuals to categorize information, generalize knowledge across tasks, and imagine and simulate personal future events (Addis et al., 2007; McClelland et al., 1995).

**Overgeneral Memory Bias**

An autobiographical memory bias that has not been widely studied but is slowly gaining traction in chronic pain research concerns differences in autobiographical memory specificity (Liu et al., 2014; Quenstedt et al., 2021; Siqveland et al., 2019; Vucurovic et al., 2019). According to the Self-Memory System model of autobiographical memory organization (Conway & Pleydell-Pearce, 2000), memories are stored and retrieved in a hierarchy of levels of representation that is arranged from general to specific. During recollection, the memory search begins at the highest, most general level of conceptual themes and lifetime periods (e.g., “my twenties”) before proceeding to intermediately general memories of repeated (e.g., “every time I stub my toe”) and extended (“My back ached for a week after my surgery”) events, and ultimately ends with the lowest tier of the hierarchy which is event-specific knowledge (“I felt relieved and pain-free the day I left the hospital”). The habitual tendency not to recollect specific memories from the final level is known as an overgeneral memory bias (OGM). This phenomenon is well-established in mental health disorders such as depression, PTSD, and complicated grief (Brown et al., 2013; Maccallum & Bryant, 2008; Sutherland & Bryant, 2008).

Common tools for assessing autobiographical memory specificity typically involve tasks that assess participants' ability to freely recall specific events, sometimes in response to neutral or emotional cue words or incomplete sentence stems. Memory responses are then coded for the presence or absence of a temporally specific event and the number of each type of memory is summed to yield a composite score that represents the overall degree of specificity or OGM in an individual's retrieval style.

**Overgeneral Memory Bias in Chronic Pain**

To our knowledge, only a handful of studies have examined OGM in individuals with chronic pain, all of which employed cross-sectional designs (Liu et al., 2014; Quenstedt et al., 2021; Siqveland et al., 2019; Vucurovic et al., 2019). Three of these identified an OGM bias in chronic pain patients (Liu et al., 2014; Quenstedt et al., 2021; Vucurovic et al., 2019) whereas the fourth (Siqveland et al., 2019) did not, largely because of methodological problems described below.

Liu et al. (2014) administered the Chinese version of the Autobiographical Memory Test (AMT) to a sample of 170 healthy controls and 176 outpatients with heterogenous chronic pain conditions for a minimum of 6 months. Participants were asked to describe the first specific personal event that came to mind in response to seeing positive and negative cue words. In line with the standard AMT protocol, nonspecific responses were followed by a probe from the experimenter. After controlling for symptoms of depression and anxiety, compared to the healthy controls, participants who had chronic pain generated a greater number of overgeneral memories independent of cue type. Accounting for the same covariates, outpatients also showed slower overall retrieval latency (time to initial response) with a non-significant trend toward slower response times for positive than negative cue words. As would be expected, chronic pain patients had significantly more symptoms of depression and anxiety, and lower pain self-efficacy scores predicted OGM across all patients. The authors concluded that the patients with chronic pain displayed distortions in AM, which, together with the statistically not significant delay in accessing positively-cued memories, reflects an affective avoidance mechanism for regulating negative emotionality. Thus, individuals with chronic pain might find it more difficult to confront experiences associated with intense or negative emotions and therefore avoid recalling these specific memories.

Quenstedt et al. (2021) used an online version of the Sentence Completion for Events from the Past Test (Raes et al., 2007) and a future-oriented equivalent (Anderson & Dewhurst, 2009) to assess specificity in chronic pain patients' memories and future imagination, respectively. Eighty-four participants with self-reported chronic pain and 102 self-identified healthy controls generated specific memories and plausible personal future events in response to neutral sentence stems. Controlling for symptoms of depression and anxiety, the results not only corroborated previous findings of an overgeneral memory bias in individuals with chronic pain when recollecting the past, but they also showed the novel finding of an overgeneral bias when imagining personal events in the future. This observation aligns with the previously mentioned notion that the cognitive processes involved in future thinking overlap with those that underlie autobiographical memory (Addis et al., 2007; Gamble et al., 2019; Schacter & Addis, 2007). The authors of this study did not report correlations between performance on the memory and future thinking tasks. However, given what is known about the role of autobiographical memory processes in shaping our self-representations and future goals, it is likely that these same processes play an important role in healing and recovery from chronic pain (Jing et al., 2016).

The third study, by Vucurovic et al. (2019), investigated patients with fibromyalgia (> 6 months' duration) and their self-defining memories (SDM): a subset of autobiographical memories that correspond to one's sense of identity and establish continuity in our personal life narratives. These memories are vivid and well-rehearsed, often encompassing an individual's central goals in life and internal conflicts (Conway et al., 2004; Singer & Moffitt, 1991). The results showed that relative to healthy controls, fibromyalgia patients exhibited significantly increased OGM (among other memory differences discussed in a subsequent section).

The fourth study recruited a Norwegian sample of 43 patients with diverse chronic pain conditions and compared those with and without PTSD on autobiographical memory using the AMT (Siqveland et al., 2019). In contrast to Liu et al. (2014), the results failed to show differences between the two groups or a significant relationship between the extent of pain and memory specificity, although it did reveal another type of memory bias in which the memories were of more negative emotionality. The study by Siqveland et al. (2019) has several limitations, acknowledged by the authors themselves, that might explain the absence of differences in autobiographical memory. First, the sample size was very small, potentially precluding sufficient power to detect real effects. Moreover, the participants in the study had moderate-to-severe chronic pain. As a result, it's possible that the entire sample may have had more overgeneral memories which would not have been detected due to the absence of a healthy control group.

Taken together, these findings suggest that people living with a chronic pain condition such as fibromyalgia might experience certain distortions in their sense of self that contribute to the maintenance of their pain. Overall, with one exception, the few published studies suggest that OGM plays an important role in chronic pain, with some evidence extending to individuals' identities, emotional self-regulation abilities, and future imaginings.

### Biases in Autobiographical Memory Content Related to Pain and Surgery

Cross-sectional studies on autobiographical memory have found that individuals with various chronic pain conditions tend to recall more pain-related content (Quenstedt et al., 2021; Wright & Morley, 1995) and exhibit a bias in which they recall memories with more negative emotional valence (Meyer et al., 2015; Siqveland et al., 2019). In regard to valence, it has been suggested that it is current pain, not chronic pain per se, that contributes to negative emotionality (Meyer et al., 2015). An early study by Wright et al. (1995) found that in a small sample of patients with chronic pain, memories comprised of pain-related information were accessed more quickly by patients than healthy controls. In addition, as previously mentioned, self-defining autobiographical memories in patients with fibromyalgia were more negative but less intense than healthy controls (Vucurovic et al., 2019). Unlike the other studies, patients did not differ in the amount of pain-related content. Taken together, these findings support Bower's Network Theory of Emotion and Memory that outlines state dependency and mood congruency, in which an individual's current emotional state enables less effortful access to memories of similar content and emotionality (Bower, 1981).

## Objectives and Hypotheses

Until now, longitudinal studies in adults have not been conducted to evaluate the temporal relationship between autobiographical memory and the development of chronic pain over time including after major surgery. This project sought to address these gaps by investigating autobiographical memory before and after major surgery using a prospective longitudinal design. Presurgical memory specificity, content, and latency were analyzed in relation to pain across multiple postsurgical timepoints that spanned one year. It was hypothesized that 1) an overgeneral memory style, 2) a bias toward surgery-related content, and 3) more negatively-valenced memories would separately predict the development of CPSP; 4) There were no specific predictions about retrieval latency of autobiographical memories.

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# Autobiographical Memory Predicts Postsurgical Pain up to 12 Months after Major Surgery

Research Paper

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## Autobiographical memory predicts postsurgical pain up to 12 months after major surgery

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**Abstract**

Recent cross-sectional studies have identified differences in autobiographical memory (AM) among individuals with chronic pain, but the temporal relationship between the 2 is unknown. Moreover, AM has yet to be studied in patients undergoing major surgery. This study addressed these gaps by conducting a prospective, longitudinal study of memory performance, postsurgical pain, and psychosocial factors in 97 adult participants scheduled for major surgery. Memories were evaluated using the Autobiographical Memory Test before and one month after surgery when participants were asked to recall personal events related to positive and pain-related word cues. Responses were coded for level of specificity, emotional valence, and surgery-related content. Questionnaires assessing presence/absence of pain and psychological functioning were administered before and at 1-, 3-, 6-, and 12-month follow-ups. Generalized estimating equations modelled pain at each postsurgical time point with memory variables as predictors. As hypothesized, higher numbers of specific pain memories recalled before surgery predicted lower odds of pain across all time points (OR = 0.58, 95% CI [0.37-0.91]). Participants who took longer to recall pain memories before surgery (OR = 2.65, 95% CI [1.31-5.37]) and those who produced more surgery-related content at the one-month assessment (OR = 1.31, 95% CI [1.02-1.68]) had greater odds of reporting postsurgical pain up to 12 months later. These findings indicate that presurgical AM biases are risk factors for development and maintenance of postsurgical pain. To the extent that these biases are causal, presurgical interventions that modify the quality and content of patients' memories may prove to be promising strategies in the prevention of chronic postsurgical pain.

**Keywords:** Chronic pain, Chronic postsurgical pain, Surgery, Risk factors, Psychological distress, Memory, Autobiographical memory, Memory bias, Overgeneral memory, Memory specificity

### 1. Introduction

Chronic postsurgical pain (CPSP) is a surgical complication characterized by pain that persists beyond normal healing time.[57] Chronic postsurgical pain occurs in 10% to 70% of patients depending on the surgical procedure[18,20,25] and is responsible for approximately 25% of referrals to chronic pain clinics.[13] The need to prevent and effectively manage CPSP is critical, given its alarming prevalence worldwide and its incidence, which adds millions of new cases to the roster each year.[25,38,65] Identifying causal, modifiable risk and protective factors for CPSP can facilitate this goal and advance our overall understanding of the transition from acute to chronic pain.[25,51]

In addition to its debilitating physical sequelae, chronic pain is associated with alterations in memory, especially that of pain.[27,44,45] One area that warrants attention for its potential role in initiating and maintaining chronic pain is autobiographical memory. Autobiographical memory refers to a system of memories for one's personal past consisting of episodic and semantic components. The coherent and flexible construction of these memories is integral to one's sense of self-continuity[23,65] and well-being,[12,17] facilitating everyday behaviours such as planning and imagining the future,[1,2] problem-solving,[59,64] and emotional regulation.[53] A phenomenon known as overgeneral memory describes a tendency to recollect personal memories that lack specificity.[73] It has been proposed that psychological processes of rumination and avoidance, also common in chronic pain, interfere with the search for event-specific knowledge and cause retrieval to fixate at the overgeneral level.[75] Although an overgeneral bias is well established in mood disorders,[47,76] relatively little is known about autobiographical memory in chronic pain.

Cross-sectional research on the topic yields mixed findings. Some studies have found greater overgenerality[30,52,71] and differences in retrieval latency among individuals with chronic pain compared with pain-free controls.[30,77] Quenstedt et al.[52] extended these findings by showing that individuals with a history of chronic pain have similar patterns of reduced specificity as well as more pain-related content in their recollections and imagined future episodes. These observations align with findings that individuals with chronic pain tend to retrieve memories with congruent emotionality and content.[39,77] By

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contrast, another cross-sectional study failed to find associations between memory specificity and chronic pain but did report state-dependent differences in memory valence.[60] However, because not one prospective study has evaluated memory specificity and its association with pain, the temporal relationship between the 2 remains unknown, and hypotheses about determinant factors cannot be ruled out. Moreover, to our knowledge, memory specificity and its relation to pain have not been examined in individuals undergoing major surgery.

This study sought to address these gaps. We assessed autobiographical memory before and after major surgery using a prospective longitudinal design. Presurgical memory specificity, content, and latency were analyzed in relation to pain across multiple postsurgical time points that spanned one year. We hypothesized that an overgeneral memory style, a bias toward surgery-related content, and more negatively valenced memories would individually predict the development of CPSP. We did not have specific predictions about retrieval latency.

## 2. Methods

### 2.1. Participants

One hundred nine patients scheduled to undergo major surgery at the Toronto General Hospital were approached for the study. Inclusion criteria were patients scheduled for major surgery; to receive intravenous or epidural opioids postoperatively for a minimum of 48 hours; age between 18 and 60 years; and fluency in English. Patients who were scheduled for other regional anaesthetic techniques during or after surgery were not eligible for participation in the study.

### 2.2. Procedure

The study was reviewed and approved by the Research Ethics Boards at Toronto General Hospital (06-0641-AE) and York University (2006-240). Patients were recruited for the study during their preadmission appointment an average of 8.85 $\pm$ 6.11 days before surgery. After obtaining informed consent, a set of presurgical questionnaires assessing demographic, health, pain, and psychosocial information were administered. Patients were followed-up on these measures and other pain-related questions in person one month after surgery, whereas 3-, 6-, and 12-month follow-ups were completed by telephone. Questionnaires administered as part of a separate research question concerning psychosocial predictors of CPSP included the PTSD Checklist Civilian Version,[72] Pain Catastrophizing Scale,[62] Fear of Pain Questionnaire-III,[37] and Pain Anxiety Symptoms Scale (PASS-20).[36] Seeing as we did not have a priori hypotheses about these measures, they were not analyzed for the current sample and only questionnaires pertinent to the study were included in the final analyses and discussed below. The Autobiographical Memory Test was administered to participants in person by a research nurse during the preadmission appointment as well as one month after surgery (40.45 $\pm$ 17.52 days). At each follow-up assessment, we attempted to contact participants by telephone a maximum of 3 times and a voice message was left on the third call. Those who could not be reached were deemed lost to follow-up.

### 2.3. Measures

#### 2.3.1. Pain

Pain in the current study was defined dichotomously, by its presence or absence. Classification of patients into pain or nonpain groups was based on questions from the Current Pain and Pain History Questionnaire[49] administered at baseline and pain-related questions from surveys conducted at each postsurgical follow-up interview. At baseline, participants specifically responded to the question, "Do you have any ongoing pain problems?". Those who responded "yes" were categorized as having baseline pain before surgery. For each postsurgical interview, participants responded to questions about their postsurgical pain, including "Are you in pain right now?" and "Are you ever in pain?". If they answered "yes" to either question, they were categorized as having pain at that particular time point. Of the 100 pain values that were missing across the 4 postsurgical time points, 39 of these were inferred based on patients' responses to the same question at subsequent time points (eg, if time point 2 was missing but the responses at time point 3 and 4 were "yes", time point 2 was recorded as "yes") and/or based on their responses about the length of time it took for pain to disappear after surgery.

Seeing as most studies to date have linked memory biases to the experience of pain, pain presence was chosen over other clinically relevant measures such as pain disability. The focus on pain might also in part be attributed to the brain regions presumed to be common to memory and pain. The hippocampus, which is known for its key role in processing autobiographical memories, has recently been found to undergo changes that have predictive implications for chronic pain.[3,6,42,69] Expansion of the left posterior hippocampus has also been shown to be associated with negative memory biases in patients with chronic pain reflected in a tendency to recall pain as more intense than originally reported.[6] Therefore, we expected memory biases in this study to be linked to the experiential components of pain, which seem to relate to the mechanism that links memory and pain.

#### 2.3.2. Hospital anxiety and depression scale

The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report measure that screens for anxiety and depression.[79] Participants are asked to rate each item on a 4-point scale ranging from 0 to 3 based on how they have been feeling in the past week. Half the items assess for symptoms of depression, namely anhedonia, slowing down, and appearance, whereas the other half screen for anxiety reflected through feelings of tension, restlessness, and autonomic anxiousness. Responses for each subscale item are summed to yield separate anxiety (HADS-A) and depression (HADS-D) scores. The current study also used the HADS total score, which has been found to be a good estimate of a strong general factor representing general psychological distress[46] validated in patients with chronic pain.[19,31] Higher scores indicate greater severity of emotional distress. The HADS total score and subscales have been shown to have good psychometric properties in patients with acute and chronic pain, including high internal reliability (HADS-A: mean $\alpha$ = 0.83; HADS-D: $\alpha$ = 0.82) and good construct validity.[7,31,67] The HADS also had similar good internal reliability in our sample (HADS-A: $\alpha$ = 0.86; HADS-D: $\alpha$ = 0.81; HADS-Total: $\alpha$ = 0.89).

#### 2.3.3. Autobiographical Memory Test

The Autobiographical Memory Test (AMT)[73] is the most commonly used measure of overgeneral memory. Few studies report the internal consistency of the AMT, possibly because of the underestimation of reliability for binary data when examined using traditional statistical measures such as Cronbach alpha.[22,56] Reported values typically range from $\alpha = 0.54$ to 0.77,[22,63] with higher reliability coefficients associated with alternative statistical methods for dichotomous items.[21,22] In this study, participants were instructed to describe the first memory that came to mind of a specific event from their past associated with the presented cue word, which was read aloud by the research nurse. They were also asked to indicate the date and time when the event occurred. If the patient failed to generate a response after 15 seconds, they were prompted again for a specific memory. Cumulative response times were recorded by the experimenter. Cues consisted of 5 pain-related words (ie, pain, hurt, sore, aching, and throbbing) and 5 positive words (ie, pleasure, safe, delighted, relieved, and relaxed), which were selected using the American Heritage Word Frequency Book and matched based on their frequency (F) and standard frequency index.[10] Word pairings and their frequencies are summarized in the Supplementary Table (available at http://links.lww.com/PAIN/B616). The order of the cues was randomized for each participant, but words were always grouped according to cue type (ie, pain-related or positive). Three neutral cue words (ie, egg, beach, and clock) were administered at the start of the task so that participants could practice generating memories and clarify instructions if necessary. In the present context, memories elicited in response to pain-related cues are referred to as pain memories.

#### *2.3.3.1. Autobiographical memory test scoring*

Specificity coding was completed using the standard method in which participants' responses were classified as either specific or nonspecific/overgeneral.[73] The specific category was composed of events that occurred within a distinct spatiotemporal context and lasted less than 24 hours (eg, "My hips were aching Sunday from stretching"), whereas nonspecific/overgeneral responses were those that described events extending beyond a single day (eg, "I've been relaxed the last 3 weeks while I was away on a cruise"), categories of repeated events (eg, "Every time I play squash my legs are always sore the next day"), personal semantic information about the self (eg, "My sister Amy has broken her arm before"; "I've always been quite sensitive"), and general semantic knowledge and associates (eg, "Dogs"; "Ottawa is the capital of Canada"). Responses that were incomprehensible, metacognitive, hypothetical, future- or present-oriented, repetitions, or nonresponses were coded as errors and omitted from the analyses. Two hundred thirty-five out of a total of 1872 responses (across both time points) were coded as errors and omitted. The number of specific and nonspecific/overgeneral responses were tallied for each cue type and used in the final analyses. A primary rater first coded all baseline memories and then met with a second rater undergoing training to review coding decisions. After the second rater completed training, both raters independently coded all memories from the second time point and achieved 79.3% agreement ($\kappa = 0.586$, $z = 14.3$, $P < 0.001$). Raters reviewed all scoring decisions together and resolved discrepancies through discussion until a consensus was reached. They were also blind to participant information including patients' pain status.

Emotional valence was coded by assigning qualitative ratings of positive, negative, or neutral emotionality to each memory. Surgery-related content was assessed by dichotomously coding memories for the presence or absence of any mention of surgery. Valence and content ratings for all memory responses were independently coded, and interrater reliability was high (valence: 93.6% average agreement, $\kappa = 0.593$, $z = 29.6$, $P < 0.001$; surgery content: 96.7% average agreement, $\kappa = 0.867$, $z = 34.2$, $P < 0.001$). Raters then met to review all coding decisions and resolved discrepancies through discussion until a consensus was reached. Final numbers for each item were totaled and used in the data analyses.

### *2.4. Statistical analyses*

Analyses were conducted using SPSS (version 27) and R Studio (version 4.0.2 for Mac). A type I error rate of 0.05 was used for all tests of significance. Differences between participants with and without pain at baseline on psychological measures at baseline were assessed using two-sample Mann–Whitney–Wilcoxon tests. Relationships between HADS-A, HADS-D, HADS total score, and memory specificity variables for each cue type at baseline were assessed using Spearman rank–order correlations.

Four generalized estimating equations (GEE) with a logit link function were used to model pain as a repeated binary outcome at 1, 3, 6, and 12 months after surgery with presurgical pain status (yes or no), time (1, 3, 6, and 12 months), and memory variables from the AMT as predictors, and baseline general distress (HADS total score), age, and sex as covariates. Memory variables were baseline specificity categories for each cue type (specific-pain cued, specific-positive cued, overgeneral-pain cued, and overgeneral-positive cued) in the first model, baseline average reaction times for each cue type in the second, baseline valence ratings (positive, negative, and neutral) in the third, and total surgery-related memories from baseline and 1 month in the fourth. Results are presented as odd ratios (OR) and the associated 95% confidence intervals (CI). Figures depict estimated marginal means and the associated 95% CIs.

## 3. Results

### *3.1. Participant characteristics*

Of the 109 patients approached, 2 were excluded because of lack of proficiency in English, one refused participation, 2 were not included because of the cancellation of the surgery, 2 withdrew the consent after surgery, and 5 additional patients were not included in the analysis as they did not return the preadmission questionnaires. The final sample therefore included 97 participants (one with information missing for sex). Out of 96 participants with available demographic information, 37 were female and 59 were male. The mean ± SD age of participants was 55.2 ± 10.8 years with a range between 19 and 73 years. The average body mass index (BMI) was 28.52 ± 5.23 kg/m$^2$ (n = 95). The majority of participants identified as White (86 out of 94) and almost half had an undergraduate or college degree (44 out of 96). Additional participant demographic characteristics are reported in **Table 1**. Information regarding the types of surgical procedures patients underwent was collected for 87 individuals and is reported in **Table 2**. Eighty-two patients out of 95 had a prior history of surgery. Thirty-seven out of 94 patients reported ongoing presurgical pain and 27 out of 95 previously had pain that persisted for more than a month. Finally, 29 out of 96 individuals were currently taking pain medications. Participant pain characteristics are summarized in **Table 2**.

Thirty-nine instances of missing pain status values (10.1% of the total dataset) across the 4 postsurgical time points were imputed using the method described above. Missing memory data and pain values that could not be replaced were omitted from the final analyses, leaving 88 cases for the GEE analyses.

Table 1

**Participant demographic characteristics assessed before surgery.**

| Demographic characteristics | Completers | n |
|---|---|---|
| Sex, n (%) | | 96 |
| Female | 37 (38.54%) | |
| Male | 59 (61.46%) | |
| Age, M ± SD | 55.20 ± 10.79 | 95 |
| BMI, M ± SD | 28.52 ± 5.23 | 95 |
| BMI, n (%) | | |
| Underweight 18.5 kg/m$^2$ | 0 (0%) | |
| Normal 18.5-24.9 kg/m$^2$ | 25 (26.32%) | |
| Overweight 25-29.9 kg/m$^2$ | 39 (41.05%) | |
| Obese 30 kg/m$^2$ | 31 (32.63%) | |
| Ethnicity, n (%) | | 94 |
| African-Canadian | 5 (5.32%) | |
| South Asian | 1 (1.06%) | |
| Middle Eastern or North African | 1 (1.06%) | |
| White | 86 (91.49%) | |
| Hispanic/Latino | 1 (1.06%) | |
| Highest level of education completed, n (%) | | 96 |
| Elementary | 10 (10.42%) | |
| High school | 22 (22.92%) | |
| Undergraduate university or college degree | 44 (45.83%) | |
| Graduate university degree | 20 (20.83%) | |

Table 2

**Participant pain characteristics assessed before surgery.**

| Pain characteristics | Completers | n |
|---|---|---|
| Type of surgery, n | | 87 |
| Gynecological | 9 | |
| Urologic surgery | 38 | |
| Breast reconstruction/mastectomy | 5 | |
| General (Abdominal) surgery | 5 | |
| Thoracic surgery | 13 | |
| Other (orthopedic, plastic, vascular, and neck) | 17 | |
| Previous surgery? n (%) | | 95 |
| Yes | 82 (84.54%) | |
| No | 13 (13.40%) | |
| Do you have any ongoing pain problems? n (%) | | 94 |
| Yes | 37 (38.14%) | |
| No | 57 (58.76%) | |
| Have you ever had a pain problem that persisted for more than 1 mo? n (%) | | 95 |
| Yes | 27 (27.83%) | |
| No | 68 (70.10%) | |
| Are you currently taking any pain medications? n (%) | | 94 |
| Yes | 29 (29.90%) | |
| No | 65 (67.01%) | |

Comparisons between individuals with and without pain at each time point revealed that patients with ongoing pain had significantly higher baseline scores on anxiety (pain: 8.22 ± 4.56; no pain: 6.54 ± 3.72), depression (pain: 4.81 ± 3.46; no pain: 2.72 ± 2.83), and general psychological distress (pain: 13.03 ± 7.47; no pain: 9.26 ± 6.01), all $P < 0.05$. There were no significant associations between the psychological measures and memory specificity variables, all $P > 0.05$ (**Table 3**).

### *3.2. Generalized estimating equations analyses with memory variables*

#### *3.2.1. Memory specificity*

Across all postsurgical time points, the number of specific pain memories (memories generated in response to pain-related cues) recalled at baseline was associated with lower odds of having pain at follow-up ($\chi^2_{wald}$ = 5.67, OR = 0.58, $P$ = 0.017, 95% CI [0.37-0.91]) (**Fig. 1**). The confidence interval is relatively narrow, indicating a more precise estimate. The main effects of time and presurgical pain were significant, indicating that the percentage of individuals with pain decreased over time (1 month: $\chi^2_{wald}$ = 42.098, OR = 15.64, $P < 0.001$, 95% CI [6.81-35.89]; 3 months: $\chi^2_{wald}$ = 13.01, OR =3.95, $P < 0.001$, 95% CI [1.87-8.34]; 6 months: $\chi^2_{wald}$ = 4.33, OR = 2.00, $P$ = 0.037, 95% CI [1.04-3.85]) and that presurgical pain was positively associated with postsurgical pain at all time points ($\chi^2_{wald}$ =6.85, OR = 2.86, $P$ = 0.009, 95% CI [1.30-6.27]), respectively. The confidence interval for the main effect of time at 1 month was quite wide, whereas the other intervals are relatively narrow, indicating a more precise estimate. Two-way and 3-way interactions among memory variables, time, and presurgical pain were not significant.

#### *3.2.2. Memory reaction times*

Reaction times were ln-transformed to adjust for violations of normality gauged from histogram plots and significant Shapiro–Wilk tests ($P < 0.05$). Longer reaction times for pain-related cues were associated with greater odds of developing postsurgical chronic pain ($\chi^2_{wald}$ = 7.40, OR = 2.65, $P$ = 0.007, 95% CI [1.31-5.37]) (**Fig. 2**). The confidence interval is relatively narrow, indicating higher precision. There were also main effects in which the percentage of individuals with pain decreased over time and baseline pain was positively associated with postsurgical pain across all time points, both $P < 0.05$.

#### *3.2.3. Memory valence*

Baseline valence ratings were not predictive of pain at any of the postsurgical time points. Main effects of time and baseline pain, however, remained significant, both $P < 0.05$.

#### *3.2.4. Surgery-related memory content*

Because of a large percentage of missing HADS data at 1 month (41.5%), the measure was not included as a covariate in this model. More surgery-related memory content generated at the 1-month assessment predicted higher odds of pain across all postsurgical time points ($\chi^2_{wald}$ = 4.38, OR = 1.31, $P$ = 0.036, 95% CI [1.02-1.68]) (**Fig. 3**). Precision of this estimate is relatively high, given the narrow confidence interval. There was no main effect of surgery content from presurgical memories. Main effects of time and baseline pain remained significant.

## 4. Discussion

Research shows that individuals with chronic pain tend to exhibit an overgeneral memory bias (OGM) characterized by personal recollections that lack specificity. However, because of the cross-sectional nature of prior work, the temporal relationship between chronic pain and OGM has, heretofore, been unknown. This study examined autobiographical memory (AM) as a risk/protective factor for CPSP. As hypothesized, the results show that fewer specific pain-related AMs recalled before major

**Table 3**

**Means, SDs, and Spearman rank–order correlations between HADS (anxiety, depression, and total scores) and memory specificity variables at baseline (T0).**

| Variable | M | SD | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|
| 1. T0 pain-specific | 1.53 | 1.31 | | | | | | |
| 2. T0 pain-nonspecific | 2.64 | 1.28 | −0.71*** | | | | | |
| 3. T0 positive-specific | 1.94 | 1.38 | 0.42*** | −0.25* | | | | |
| 4. T0 positive-nonspecific | 2.53 | 1.36 | −0.29** | 0.28** | −0.84** | | | |
| 5. T0 HADS-A | 7.16 | 4.13 | 0.02 | 0.10 | 0.03 | 0.00 | | |
| 6. T0 HADS-D | 3.54 | 3.22 | −0.08 | 0.15 | 0.01 | 0.06 | 0.65*** | |
| 7. T0 HADS total | 10.69 | 6.82 | −0.02 | 0.13 | 0.03 | 0.01 | 0.92*** | 0.88*** |

M and SD are used to represent mean and standard deviation, respectively. *$P < 0.05$. **$P < 0.01$. ***$P < 0.001$.

surgery significantly predicted pain status 1, 3, 6, and 12 months later. These results build on previous research by demonstrating that the degree of specificity in individuals' recollections, particularly pertaining to pain, predicts CPSP status across the first year after surgery, even after controlling for known confounders including baseline pain status, general psychological distress, age, and sex. In addition, participants who took longer to retrieve pain-related memories before surgery as well as those who recalled more surgery-related content during the acute postsurgical phase were more likely to report pain up to one year later. Contrary to our predictions, we did not find any differences in presurgical memory valence between patients who did and did not develop CPSP. Consistent with the literature, baseline pain also emerged as a risk factor for the development of CPSP.[24,25]

Notably, the prospective nature of this study indicates that the relative paucity of specific autobiographical pain memories recalled before surgery is a risk factor for the development and maintenance of chronic pain status up to 1 year after major surgery. According to Conway's self-memory system,[11] AMs are accessed through an effortful generative retrieval process that progresses in a hierarchical manner beginning with conceptual themes and lifetime periods, followed by general memories of repeated and extended events, and ultimately ending with event-specific knowledge restricted to a particular spatiotemporal context. Processes involving rumination, functional avoidance, and limitations in executive control are posited to contribute to OGM by truncating this search process.[75,76] Although this model has predominantly been tested in emotional disorders, similar mechanisms might apply to OGM in patients scheduled for major surgery who develop CPSP.

Indeed, cognitive-affective biases play an important role in chronic pain.[40,50] For individuals who are particularly susceptible to psychological and emotional distress, self-relevant cues (eg, pain-related words) might interrupt the search for a specific memory by activating iterative retrievals of conceptual pain memories that coincide with rumination and potentially interfere with inhibitory control. It is possible that this sort of abstract thinking perpetuates a maladaptive self-concept centered around pain that, upon repeated activation, triggers a cascade of psychological consequences and ultimately predisposes individuals to more severe pain outcomes.[41,50] Conversely, a tendency to retrieve specific events and their experiential details might allow for greater contextualization of self-relevant pain information and provide evidence that can disprove dysfunctional pain-related beliefs. Confronting one's pain in this way can aid in coping and recuperation.

It is also possible that memory processing in surgical patients might be limited to the OGM level because of their evasion of specific pain memories associated with intense or negative emotions. Pain-related anxiety and traumatic stress responses, including avoidance of pain-related situations, are common antecedents to pain chronicity and disability.[4,26] Several studies have found that attentional avoidance of certain pain-related stimuli predicts the development of postoperative and chronic pain.[28,58] Importantly, in this study, OGM predicted CPSP even after controlling for the effects of other psychosocial factors. Therefore, these results suggest that the observed reduction in specificity is likely not attributable to underlying psychopathology. Further work is needed to clarify the role of dysfunctional emotional, cognitive, and executive processes, and their contributions to overgeneral pain memories in patients undergoing major surgery. Investigating these biases simultaneously can elucidate whether and how these mechanisms interact to influence memory and subsequent pain outcomes.[70]

This study also adds to previous research by demonstrating that participants who took longer to access pain memories before surgery were at greater risk of developing CPSP up to one year later. These findings suggest that access to personal pain memories for these individuals was more effortful and less direct, requiring the use of generative memory processes.[68] As discussed above in relation to OGM, limited access to these memories might inhibit individuals' ability to properly process past pain experiences and result in unfavorable outcomes. Cross-

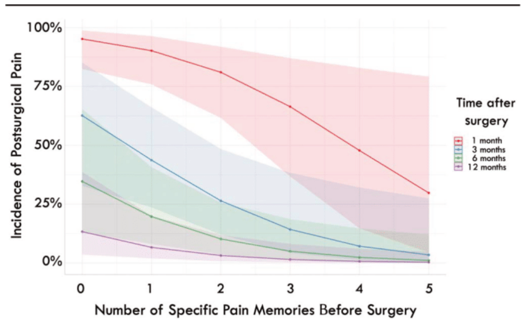


**Figure 1.** Incidence of pain at postsurgical follow-ups based on the number of baseline-specific memories generated in response to pain-related cue words. Note. The plot depicts estimated marginal means. Error bands represent 95% confidence intervals.

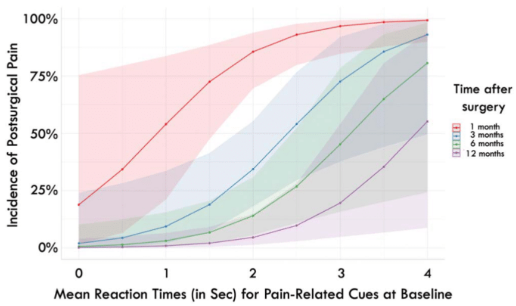


**Figure 2.** Incidence of pain at postsurgical follow-ups based on the average reaction times in response to pain-related cue words at baseline. Note. The plot depicts estimated marginal means. Error bands represent 95% confidence intervals.

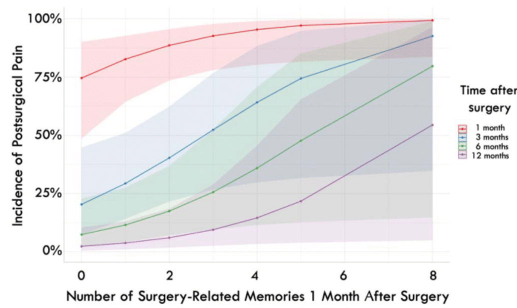


**Figure 3.** Incidence of pain at postsurgical follow-ups based on the number of surgery-related memories generated 1 month after surgery. Note. The plot depicts estimated marginal means. Error bands represent 95% confidence intervals.

sectional research by Liu et al.[30] similarly found that after controlling for negative affect, chronic pain outpatients showed slower AM retrieval. Other cross-sectional studies have also found shorter retrieval latency for pain-related memories[77] where pain as a negative state was interpreted to enable quicker access to memories of similar emotionality or content.[5] Considering that participants in this study were tested before the development of CPSP, however, quicker access to pain-congruent information would not necessarily be expected the way it is in individuals who have chronic pain. On the contrary, cognitive slowing might occur because of the fact that more effort is required to complete goal-directed tasks when greater demands are placed on working memory to mitigate distractions caused by preexisting pain and psychological dysfunction, which often precede CPSP.[15,35,48] Research is needed to investigate these possibilities.

Regarding memory content, the present results indicate that individuals who remembered more surgery-related memories one month after their operation were more likely to develop CPSP. This aligns with numerous studies in patients with chronic pain and other clinical populations (eg, PTSD and complicated grief) that also show a tendency to recall memories and imagine future episodes containing mood-congruent content.[9,32,39] One interpretation of these results can be gleaned from the self-memory system model of AM, which postulates that memories are shaped by an individual's current self-representation and goals.[64] As such, memories that are congruent with one's self-image are considered more accessible than those that are not.

Future research should clarify whether AM is a causal factor in the development of CPSP. If it is, the results from this study present important implications for the prevention and treatment of chronic pain.[16,51] For example, novel interventions could be developed to modify patients' presurgical memories with a focus on training individuals to selectively retrieve specific pain memories and enhance episodic reexperiencing of past events. Memory specificity training programs are effective not only for improving specificity but psychological well-being as well.[33,34,43,55] Moreover, psychotherapies used for presurgical and postsurgical pain management could be enhanced to incorporate memory reframing techniques that restructure negative pain associations. Indeed, considering that patients in this study who were vulnerable to CPSP showed a preoccupation with surgery, setting positive goals and reducing rumination could be conducive to recovery. Nonetheless, the utility of such treatments is contingent on the causal role of AM, which has yet to be determined.

This study has several limitations. First, our sample size precluded exploring interaction effects without overfitting the GEE models. Limited demographic information was collected and the sample was overwhelmingly White, which may reduce generalizability of findings. Future studies with larger and more diverse samples could examine how different types of AM biases might interact to predict CPSP. In addition, although the AMT is a very popular method for assessing OGM, elicited responses tend to be very brief, which can be difficult to reliably interpret and qualify. Moreover, entire memories are dichotomously scored according to temporal specificity. This approach contradicts cognitive models that suggest AMs simultaneously consist of both episodic and semantic details.[29,66] Memory assessment tools that allow for elaboration and use a more nuanced scoring method (eg, The Autobiographical Interview[29]) could provide insight into the types of details represented in the personal memories of surgical and chronic pain patients. Future studies might also consider using different versions of the memory task on each test occasion to control for prior exposure or practice effects. Finally, neurocognitive and psychiatric conditions were not screened for in the current sample. This would have been important for dissociating these factors from memory performance and pain. In the same vein, including objective measures of episodic and semantic memory could provide a control for general dysfunctions of declarative memory.

In summary, the results of this study indicate that differences in AM style are a risk factor for the development of CPSP. Reduced presurgical specificity for pain-related memories and a bias toward surgery-related content during the acute postsurgical phase were predictive of chronic pain after major surgery. Moreover, more effortful retrieval reflected in longer response times for presurgical pain memories also predicted worse postsurgical pain outcomes up to one year later. Future research should investigate the effectiveness of treatment strategies that take advantage of AM as a modifiable risk factor by optimizing patients' access to specific memories of past pain experiences and redirecting focus toward more constructive memory content. Contextualizing memories in this way might facilitate postsurgical recovery and present a promising new path for preventing the transition from acute to chronic pain.

## Conflict of interest statement

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## Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/B616.

## Supplemental video content

A video abstract associated with this article can be found at http://links.lww.com/PAIN/B617.

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## General Discussion

Research shows that individuals with chronic pain tend to exhibit an overgeneral memory bias (OGM) characterized by personal recollections that lack specificity. However, due to the cross-sectional nature of prior work, the temporal relationship between chronic pain and OGM has, heretofore, been unknown. This study examined autobiographical memory as a risk/protective factor for chronic postsurgical pain (CPSP). As hypothesized, the results show that fewer specific pain-related autobiographical memories recalled before major surgery significantly predicted pain status 1-, 3-, 6-, and 12-months later. These results build on previous research by demonstrating that the degree of specificity in individuals' recollections, particularly pertaining to pain, predicts CPSP status across the first year after surgery, even after controlling for known confounders including baseline pain status, general psychological distress, age, and sex. Additionally, participants who took longer to retrieve pain-related memories before surgery as well as those who recalled more surgery-related content during the acute postsurgical phase were more likely to report pain up to one year later. Contrary to our predictions, we did not find any differences in presurgical memory valence between patients who did and did not develop CPSP. Consistent with the literature (Katz, 1997; Katz & Seltzer, 2009), baseline pain also emerged as a risk factor for the development of CPSP.

The relative paucity of specific pain-related memories and longer latencies to respond by participants who went on to develop CPSP can be explained, in part, by Conway's self-memory system (Conway & Pleydell-Pearce, 2000). According to this model, autobiographical memories are accessed through an effortful generative retrieval process that progresses in a hierarchical manner beginning with conceptual themes and lifetime periods, followed by general memories of repeated and extended events, and ultimately ending with event-specific knowledge restricted to a particular spatiotemporal context. Processes involving rumination, functional avoidance, and limitations in executive control are posited to contribute to OGM by truncating this search process (Williams, 2006; Williams et al., 2007).

The cognitive processes associated with rumination, avoidance, and poor executive control, either separately or in combination, have been posited to interfere with the search for a specific memory and to cause retrieval to remain fixed at the overgeneral level of the autobiographical knowledge base (Williams, 2006). The first component of the proposed *CaRFAX* model, *capture and rumination* (CaR), occurs when self-relevant cues activate repeated retrieval of general memories thereby "capturing" the individual in a ruminative process that interferes with the search for a specific memory. Next, specific memories associated with unpleasant or intense emotional experiences are avoided to prevent activating intense and negative emotions in what is termed *functional avoidance* (FA). Finally, limitations in *executive control* (X) such as working memory and inhibition of irrelevant information can also impede event-specific retrieval. While this model has predominantly been tested in emotional disorders, it has not received much attention in the pain literature even though cognitive-affective biases play an important role in chronic pain (Moriarty et al., 2011; Pincus & Morley, 2001). Similar mechanisms might apply to OGM in patients scheduled for major surgery who develop CPSP. It is possible that individuals who are particularly susceptible to psychological and emotional distress, self-relevant cues (e.g., pain-related words) might interrupt the search for a specific memory by activating iterative retrievals of conceptual pain memories that coincide with rumination and potentially interfere with inhibitory control. The sort of abstract or general thinking associated with OGM might perpetuate a maladaptive self-concept or schema centered around pain that, upon repeated activation, triggers a cascade of psychological consequences and ultimately predisposes individuals to more severe pain outcomes (Morley et al., 2005; Pincus & Morley, 2001). Conversely, a tendency to retrieve specific events and their experiential details might allow for greater contextualization of self-relevant pain information and provide evidence that can disprove dysfunctional pain-related beliefs. Confronting one's pain in this way can aid in coping and recuperation.

It is also possible that memory processing in surgical patients might be limited to the OGM level due to their evasion of specific pain memories associated with intense or negative emotions. Pain-related anxiety and traumatic stress responses, including avoidance of pain-related situations, are common antecedents to pain chronicity and disability (Asmundson & Katz, 2009; Kleiman et al., 2011). Several studies have found that attentional avoidance of certain pain-related stimuli predicts the development of postoperative and chronic pain (Lautenbacher et al., 2009; Sharpe et al., 2014). Jones (1957) attributed the difficulty associated with remembering pain experiences to the repression of fearful events. He also posited that pain becomes increasingly difficulty to cope with over time at least in part due to the fact that subsequent experiences evoke responses to current stimulation as well as to buried memories of previous pain (Erskine et al., 1990). In their review, Erskine et al. (1990) distinguish between episodic and semantic involvement of memory in acute and chronic pain, respectively by explaining that in chronic pain, retrieval of a pain memory is more affected by an individual's global view of their pain problem including their pain identity, mood, and quality of life that relies semantic memory than the intensity or quality of the pain itself. The latter is associated more with acute pain experiences for which retrieval relies on episodic memory.

Importantly, in the present study, OGM predicted CPSP even after controlling for the effects of other psychosocial factors. Therefore, these results suggest that the observed reduction in specificity is likely not attributable to underlying psychopathology. Further work is needed to clarify the role of dysfunctional emotional, cognitive, and executive processes and their contributions to overgeneral pain memories in patients undergoing major surgery. Investigating these biases simultaneously can elucidate whether and how these mechanisms interact to influence memory and subsequent pain outcomes (Van Ryckeghem & Vervoort, 2016).

The present study also adds to previous research by demonstrating that participants who took longer to access pain memories before surgery were at greater risk of developing CPSP up to one year later. These findings suggest that access to personal pain memories for these individuals was more effortful and less direct, requiring the use of generative memory processes (Uzer, 2016). As discussed above in relation to OGM, limited access to these memories might inhibit individuals' ability to properly process past pain experiences and result in unfavorable outcomes. Cross-sectional research by Liu et al. (2014) similarly found that after controlling for negative affect, chronic pain outpatients showed slower autobiographical memory retrieval. Other cross-sectional studies have also found shorter retrieval latency for pain-related memories (Wright & Morley, 1995) where pain as a negative state was interpreted to enable quicker access to memories of similar emotionality or content (Barry et al., 2004). Considering that participants in the present study were tested prior to the development of CPSP, however, quicker access to pain-congruent information would not necessarily be expected the way it is in individuals who have already developed chronic pain. On the contrary, cognitive slowing might occur due to the fact that more effort is required to complete goal-directed tasks when greater demands are placed on working memory to mitigate distractions caused by pre-existing pain and psychological dysfunction, which often precede CPSP (Dick & Rashiq, 2007; Mazza et al., 2018; Oosterman et al., 2011). Research is needed to investigate these possibilities.

Regarding memory content, the present results indicate that individuals who remembered more surgery-related memories one month after their operation were more likely to develop CPSP. This aligns with numerous studies in chronic pain patients and other clinical populations (e.g., PTSD and complicated grief) that also show a tendency to recall memories and imagine future episodes containing mood-congruent content (Brown et al., 2013; Maccallum & Bryant, 2008; Meyer et al., 2015). One interpretation of these results can be gleaned from the self-memory system model of autobiographical memory which postulates that an individual's goals and self-representations guide memory retrieval toward cognitively and emotionally compatible information (Conway & Pleydell-Pearce, 2000). As such, memories that are congruent with one's self-image are considered more accessible than those that are not. Evidence for this model largely stems from research in which individuals with various mental health disorders show a bias for recalling memories and imagining future events that match their current mood states (Brown et al., 2013). Recent findings that people with chronic pain tend to generate pain-related information when remembering the past and imagining the future further indicate that these biases might extend beyond memory and have important implications for well-being (Quenstedt et al., 2021).

Consistent with this line of thought, Pain Enmeshment Theory (Pincus & Morley, 2001) proposes that an individual's emotional adjustment to pain depends on the extent to which aspects of their self-image are "enmeshed" or intertwined with pain. This model originated from the observation that individuals with chronic pain, who also show substantial associated distress, tend to exhibit cognitive biases in attention, memory, and interpretation processes. The authors posit that these biases are the result of an overlap between the self, pain, and illness schemas. Pain Enmeshment Theory was later expanded using the framework of Self-Discrepancy Theory

(Higgins, 1987, 1997), which postulates that individuals self-regulate to account for discrepancies between different aspects of the self; namely, the actual self (aspects of the self as they currently are), the ideal self (aspects of the self as one would like them to be), and the ought self (aspects of the self that one thinks they should have). According to this model, discrepancies between the actual and ideal self are expected to lead to depression, whereas disparities between the actual and ought self lead to agitation. The authors suggested that individuals living with chronic pain are more likely to experience emotional maladjustment when they view pain as the reason why they cannot attain their desired selves. This notion was later tested and supported by Morley et al. (2005) in a study of 89 adult participants with chronic pain who reported characteristics of their current self, their hoped-for self, and their feared-for self. Participants also reported the extent to which their future selves depended on the presence or absence of pain. The results showed that the number of characteristics of the hoped-for self that were deemed attainable even in the presence of pain was negatively correlated with depression and positively correlated with pain acceptance scores (Morley et al., 2005). Thus, the more accepting a person was of their pain, the less the pain interfered with a positive self-image.

**Limitations**

The present study has several limitations. First, our sample size precluded exploring interaction effects without overfitting the GEE models. Limited demographic information was collected and the sample was overwhelmingly White, which may reduce generalizability of findings. Future studies with larger and more diverse samples could examine how different types of autobiographical memory biases might interact to predict CPSP. In addition, while the AMT is a very popular method for assessing OGM, elicited responses tend to be very brief, which can be difficult to reliably interpret and qualify. Moreover, entire memories are dichotomously scored according to temporal specificity. This approach contradicts cognitive models that suggest autobiographical memories simultaneously consist of both episodic and semantic details (Levine et al., 2002; Tulving, 1972). As discussed in the subsequent section, memory assessment tools that allow for elaboration and use a more nuanced scoring method could provide insight into the types of details represented in the personal memories of surgical and chronic pain patients. Future studies might also consider employing different versions of the memory task on each test occasion to control for prior exposure or practice effects. Finally, neurocognitive and psychiatric conditions were not screened for in the current sample. This would have been important for dissociating these factors from memory performance and pain. In the same vein, including objective measures of episodic and semantic memory could provide a control for general dysfunctions of declarative memory.

**Future Directions**

Future research should clarify whether autobiographical memory is a causal factor in the development of CPSP. If it is, results from this study present important implications for the prevention and treatment of chronic pain (Eccleston et al., 2021; Price et al., 2018). For example, novel interventions could be developed to modify presurgical memories with a focus on training individuals to selectively retrieve specific pain memories and enhance episodic re-experiencing of past events. Memory specificity training programs are effective not only for improving specificity but psychological well-being as well (Madore et al., 2016; Maestas & Rude, 2012; Neshat-Doost et al., 2013; Raes et al., 2009). Moreover, psychotherapies commonly employed for pre- and postsurgical pain management, such as CBT, could be enhanced to incorporate memory reframing techniques that restructure negative pain associations. Indeed, considering that patients in this study who were vulnerable to CPSP showed a preoccupation with surgery, setting positive goals and reducing rumination could be conducive to recovery. Nonetheless, the utility of such treatments is contingent on the causal role of autobiographical memory, which has yet to be determined.

The results of this project should also be validated using alternative methods. Most studies that investigate memory specificity, and almost all studies in chronic pain described above, assess OGM using some variation of the AMT. While the AMT is a popular and reliable tool (Griffith et al., 2012; Raes et al., 2007), it has certain limitations that should be taken into consideration and addressed in future research. First, the AMT is not considered sensitive to OGM in non-clinical populations that don't meet diagnostic criteria for mental health conditions (Griffith et al., 2012). For example, expected correlations between AMT specificity and depression scores for non-depressed individuals have been shown to be absent and, in some cases, even positive (Raes et al., 2007). It is thought that in clinically depressed individuals, an overgeneral style is the dominant mode of retrieval that with time, becomes increasingly more difficult to inhibit. However, in cases where this cognitive pattern is less potent, it might be easier for individuals to overcome, especially when they are explicitly instructed to do so in the instructions (Raes et al., 2007). As such, the typical AMT task would fail to capture these sorts of at-risk individuals.

The Sentence Completion for Events from the Past Test (SCEPT) is a more sensitive measure that was designed to address and circumvent these limitations (Raes et al., 2007). However, both tasks still require participants to provide brief descriptions of a single event, typically within a short time interval. The lack of opportunity to elaborate yields descriptions that tend to be very short, often making it difficult for scorers to reliably interpret. Furthermore, responses are scored in a dichotomous fashion where whole memories are categorized as either specific or nonspecific. This approach treats episodic and semantic components of autobiographical memory as categorically distinct and isolated systems, artificially deconstructing whole responses as belonging to either one or the other. Doing so neglects the natural co-occurrence of these two components during discourse and is not consistent with neurocognitive theories that emphasize their interdependence (Svoboda et al., 2006). Therefore, a better alternative would be to use tasks such as the Autobiographical Interview (Levine et al., 2002) which allow for elaborative, free recall and more nuanced scoring techniques that segment, categorize, and quantify details pertaining to both types of memory within a single autobiographical narrative. Such an approach could provide a more informative look into the relative patterns of deficits and preservation in individuals' pain memories in future research. If differences in the degree of episodicity exist, the underlying mechanisms driving this relationship would warrant further investigation. Based on research in emotional disorders, CaRFAX mechanisms of rumination, avoidance, and executive functioning are compelling starting points for future studies. Primarily, it is of interest to examine whether these mechanisms can explain OGM in CPSP, and if so, whether they are also meaningful contributors in non-clinical or at-risk samples. Pairing this method of memory narrative elicitation with the more common approach of comparing recall to initial pain reports using single item pain scales is important because it would further our understanding of the relationship between OGM and negative memory biases and as a result, contribute a more nuanced model of memory bias in CPSP.

Finally, considering the utility of autobiographical memory in other cognitive, emotional, and social functions, future research could explore how these other domains are affected in chronic pain, particularly in surgical patients. It is possible that certain differences might be observed in abilities that are known to necessitate intact episodic autobiographical memory processing, such as future imagination and problem-solving (Addis et al., 2007; Peters et al., 2019).

These functions are integral to establishing feelings of self-efficacy and maintaining a stable sense of self, especially in times of hardship; they enable individuals to set goals and envision attainable and positive futures for themselves. Within the context of pain, the common disruption of these functions severely hinders patients' willingness and ability to lead a full life and recover from their afflictions. As such, understanding relative difficulties in these areas could help identify new treatment targets and guide efforts aimed at preventing and managing postsurgical pain.

## Conclusion

In summary, the results of this thesis indicate that differences in autobiographical memory style are a risk factor for the development of CPSP. Reduced presurgical specificity for pain-related memories as well as a bias toward surgery-related content during the acute postsurgical phase were predictive of chronic pain after major surgery. Moreover, more effortful retrieval reflected in longer response times for presurgical pain memories also predicted worse postsurgical pain outcomes up to one year later. Future research should investigate the effectiveness of treatment strategies that take advantage of autobiographical memory as a modifiable risk factor by optimizing patients' access to specific memories of past pain experiences and redirecting focus toward more constructive memory content. Contextualizing memories in this way might facilitate postsurgical recovery and present a promising new path for preventing the transition from acute to chronic pain.

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# Appendix A

Consent

Toronto General Hospital
University Health Network

**CONSENT FORM**

**TITLE: Empirical evaluation of diathesis-stress model of chronic pain and disability after surgery**
**PRINCIPAL INVESTIGATORS: Dr. Joel Katz**
**Scientist, Department of Anesthesia and Pain Management**

**and Valery Kleiman, MA York University**

You are being asked to take part in a research study. Before agreeing to take part in this study, it is important that you read and understand the following explanation of the proposed study procedures. The following information describes the purpose, procedures, benefits, discomforts, risks, and precautions associated with this study. It also describes your right to refuse to participate or to withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should understand enough about it to make an informed decision. This is known as the informed consent process. Please ask the researcher to explain any words you don't understand before signing this consent form. Make sure all your questions have been answered to your satisfaction before signing this document.

<u>PURPOSE:</u>

You have been asked to participate in a study, which is designed to understand the relationship between fear, anxiety, and post-operative pain after surgery. We will be examining physical, psychological and emotional issues that people face before and after surgery to get a better understanding of why people respond to pain so differently while having similar types of surgery. This may help us identify or predict levels of pain people will experience after surgery and may help us develop tools or interventions aimed at reducing their pain.

<u>PROCEDURES:</u>

Participation will last one year and 230 patients will be enrolled. If you agree to participate in this study, you will first be asked to complete some questionnaires at your pre-admission hospital visit. The package of questionnaires takes about 60-80 minutes to complete, and contains questions regarding how you are feeling generally, how you have been able to manage and cope with past experiences of pain, as well as reporting any pain that you experience at present. All of the questionnaires you will be asked to complete are commonly used and they are designed to measure current and past pain experiences; pain threshold/pain tolerance; the degree to which several areas of your life are disrupted by pain; how you deal with stressful life experiences; how you have been able to cope with pain; and, how you feel in general. Upon arrival in the recovery room after your surgery an Actiwatch will be applied to your wrist and be worn at all times during your hospital stay (including while washing or showering). On the morning of the day that you are discharged to go home a member of the research team will remove the Actiwatch. The Actiwatch is a device, that looks like an actual watch that is placed on your wrist and will monitor your sleep/rest and activity. On two occasions following your surgery (24 hours and 48 hours after your surgery) you will be asked to answer some questions about how you are feeling, which will take about 20-60 minutes. In addition, the researchers will record your morphine intake for 48 hours after your surgery by using a computer program to download the information from your PCA pump. A researcher will also review your hospital chart and record pain medications given to you during your surgery, in the recovery room, and for the first 48 hours after your surgery. Examples of pain medications include tylenol, toradol, fentanyl, and advil.

One month after your surgery a researcher will meet with you during your follow-up appointment with our surgeon to conduct the follow-up assessment. You will be asked to complete the same set of questionnaires that you completed during your pre-admission visit. At three, six and twelve months after your surgery a researcher will contact you to conduct follow-up telephone interviews, again, completing the same set of questionnaires that you completed at both your pre-admission visit and your one month follow-up visit. Each of these interviews will take approximately 60-90 minutes to complete.

RISKS AND BENEFITS

There are no known personal risks or benefits associated with taking part in this research study. Information learned from this study may benefit others undergoing surgery in the future, and may further the understanding of why people respond to pain so differently while having similar types of surgery. This may help us identify or predict levels of pain people will experience after surgery and may help us develop tools or interventions aimed at reducing their pain.

CONFIDENTIALITY:

All information obtained during the study will be held in strict confidence and none of the information that we collect will be transferred out of University Health Network. The investigators, Dr. Joel Katz and Valery Kleiman, our Research Ethics Board, and direct research personnel working on this project will be the only ones who will have access to your hospital medical records (personal health information). You will be identified by a study number and initials only. No names or identifying information will be used in any publication or presentation.

PARTICIPATION:

Your participation in the study is voluntary. You may withdraw from the study at any time, and you can also choose not to answer any questions that you do not feel comfortable answering. This will not affect your medical care.

QUESTIONS:

If you have any general questions related to this study please call the Principal Investigator, Dr. Joel Katz, at . If you have any questions about your rights as a research participant, please call Dr. R. Heslegrave, Chair of the University Health Network Research Ethics Board at . This person is not involved with the research project in any way and calling him will not affect your participation in the study.

**CONSENT:**

I have had the opportunity to discuss this study and my questions have been answered to my satisfaction. I consent to participate in the study with the understanding that I may withdraw at any time without affecting my medical care. I have received a signed copy of this consent form. I voluntarily consent to take part in this study.

| | |
|---|---|
| Patient's Name (Please Print) | Subject's Signature |

Date

I confirm that I have explained the nature and purpose of the study to the subject named above. I have answered all questions.

| | |
|---|---|
| Name of Person Obtaining Consent | Signature |

Date

# Appendix B

Demographic Information

1. Sex: ☐ Male ☐ Female

2. Date of Birth: ___________
dd/mm/yyyy

3. Current age: ____________

4. Height: _____________

5. Weight: _____________

6. Ethnic Background (check as many as apply to you):
    1. ☐ African-Caribbean
    2. ☐ African-Canadian
    3. ☐ South Asian (e.g., India, Pakistan, Sri Lanka)
    4. ☐ East Asian (e.g., Hong Kong, China, Vietnam, Korea)
    5. ☐ Middle Eastern or North African (e.g., Iran, Israel, Egypt, Morocco)
    6. ☐ White
    7. ☐ Hispanic / Latino/a
    8. ☐ Aboriginal
    9. ☐ Other (please specify) ________________________________________
    ________________________________________

    In the above question, a list of ethnic backgrounds was provided. However, this list may or may not specify how you identify. Regardless of your answer to the previous question, how do <u>you</u> identify your ethnic background (s)?

    Ethnically, I identify as: ________________________________________________________

7. Degree you are pursuing at York: ____________________________________________________

8. Year of study: _____________

**Appendix C**

Current Pain and Pain History Questionnaire

**Part I. Pain History**

1. Do you have any ongoing pain problems? ☐ Yes ☐ No (Go to Question 2)

   a. If Yes, list diagnosis or type of pain and location: ________________________________
   ______________________________________________________________________________
   ______________________________________________________________________________

   b. For how long have you had the pain? ________________________________________

   c. How often do you have pain?

   - ☐ Daily
   - ☐ Weekly
   - ☐ Monthly
   - ☐ Other ______________________________________________________

   d. On the days that you feel pain, what is the average intensity of your pain?

   - ☐ Mild
   - ☐ Moderate
   - ☐ Severe

   e. How much does your pain interfere with your life?

   - ☐ Not at all
   - ☐ Slightly
   - ☐ Moderately
   - ☐ Severely

2. Do you currently feel any pain? ☐ Yes ☐ No

   a. If yes, how intensity is the pain you feel right now?

   - ☐ Mild
   - ☐ Moderate
   - ☐ Severe

   b. Where is the pain? ________________________________________________________
   ______________________________________________________________________________

3. Are you currently using any of the following pain killers or medicines? Y / N
   If yes, please check which you are taking:

   - ☐ Aspirin

- ❑ Acetaminophen (eg: Tylenol)
- ❑ NSAIDs (eg: Naproxen, Advil, Motrin)
- ❑ Opioids (eg: Tylenol # 3)
- ❑ Other ____

4. Have you ever had a pain problem that persisted for more than one month (other than what you have mentioned above)? ☐ Yes ☐ No

   Type or diagnosis and location:_______________________________________________
   ____________________________________________________________________________
   ____________________________________________________________________________
   ____________________________________________________________________________

5. Have you ever had surgery? ☐ Yes ☐ No

   If yes, please list:

| | Type of surgery | Date of surgery |
|---|---|---|
| 1. | | |
| 2. | | |
| 3. | | |

## Part II. Pain Experiences

We would like to find out about your experiences with common types of pain. Please rate the **intensity** of the following pains you may have had in the past.

Circle the number that best describes the intensity of the experience where:
1 = not at all intense and 5 = as intense as can be

Circle n/a for "not applicable" if you have never experienced the pain

| Type of Pain | Intensity (1-5) | | | | | |
|---|---|---|---|---|---|---|
| Tooth ache | 1 | 2 | 3 | 4 | 5 | n/a |
| Paper cut | 1 | 2 | 3 | 4 | 5 | n/a |
| Stubbed toe | 1 | 2 | 3 | 4 | 5 | n/a |
| Biting your tongue ........................................................ | 1 | 2 | 3 | 4 | 5 | n/a |
| Ear ache......................................................................... | 1 | 2 | 3 | 4 | 5 | n/a |

## Appendix D

Hospital Anxiety and Depression Scale

Health care professionals are aware that emotions play an important part in most illnesses. If your health care professional knows about these feelings he or she will be able to help you more.
Read each item below and place a check (✓) in the box beside the reply which comes closest to how you have been feeling in the past week.

1. **I feel tense or "wound up"**
   ☐ Most of the time
   ☐ A lot of time
   ☐ From time to time
   ☐ Not at all
2. **I still enjoy the things I used to enjoy**
   ☐ Definitely as much
   ☐ Not quite so much
   ☐ Only a little
   ☐ Hardly at all
3. **I get a sort of frightened feeling as if something awful is about to happen**
   ☐ Very definitely and quite badly
   ☐ Yes, but not badly
   ☐ A little, but it doesn't worry me
   ☐ Not at all
4. **I can laugh and see the funny side of things**
   ☐ As much as I always could
   ☐ Not quite so much now
   ☐ Definitely not so much now
   ☐ Not at all
5. **Worrying thoughts go through my mind**
   ☐ A great deal of the time
   ☐ A lot of the time
   ☐ Not too often
   ☐ Very little
6. **I feel cheerful**
   ☐ Never
   ☐ Not often
   ☐ Sometimes
   ☐ Most of the time
7. **I can sit at ease and feel relaxed**
   ☐ Definitely
   ☐ Usually
   ☐ Not often
   ☐ Not at all
8. **I feel as if I am slowed down**
   ☐ Nearly all the time
   ☐ Very often
   ☐ Sometimes
   ☐ Not at all
9. **I get a sort of frightened feeling like "butterflies' in my stomach**
   ☐ Not at all
   ☐ Occasionally
   ☐ Quite often
   ☐ Very often
10. **I have lost interest in my appearance**
    ☐ Definitely
    ☐ I don't take as much care as I should
    ☐ I may not take quite as much care
    ☐ I take just as much care as ever
11. **I feel restless as if I have to be on the move**
    ☐ Very much indeed
    ☐ Quite a lot
    ☐ Not very much
    ☐ Not at all
12. **I look forward with enjoyment to things**
    ☐ As much as I ever did
    ☐ Rather less than I used to
    ☐ Definitely less than I used to
    ☐ Hardly at all
13. **I get a sudden feeling of panic**
    ☐ Very often indeed
    ☐ Quite often
    ☐ Not very often
    ☐ Not at all
14. **I can enjoy a good book or radio or television program**
    ☐ Often
    ☐ Sometimes
    ☐ Not often
    ☐ Very seldom