Until “divorce” do us part: A mixed-method study of the experience and treatment of adjustment disorder stemming from romantic partner betrayal

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Table of Contents

List of Tables

List of Figures

Abstract

Although mounting evidence indicates that some individuals betrayed by a romantic partner may develop an adjustment disorder, a trauma-and stressor-related disorder characterized by intrusions, avoidance, and failure to adapt, there currently exists no systematic individualized treatment. Considering trauma-and stressor-related disorders as etiologically rooted in the emotional memory of a distressing life event, reducing the salience of this memory may provide a positive therapeutic outcome. Pre-clinical evidence has demonstrated that administering propranolol, a noradrenergic beta-blocker, prior to the reactivation of an emotional memory can interfere with its reconsolidation, i.e., the restabilization of memory to long-term storage. In clinical populations with posttraumatic stress disorder, this procedure, referred to as reconsolidation therapy, attenuates symptoms of traumatic stress. However, no research to date has investigated whether reconsolidation therapy can be extended to other stressor-related disorders. The first two manuscripts of this dissertation present the rationale, methods, and results of a clinical trial aimed at investigating the effectiveness of reconsolidation therapy to treat adjustment disorders stemming from romantic partner betrayal. Results from ANCOVAs revealed that compared to a no-treatment waitlist control condition (n = 29), reconsolidation therapy (n = 30) produced a significant reduction in event-related stress symptoms, including intrusions, avoidance, and increased vigilance, as well as general psychological distress, including symptoms of depression and anxiety, as measured with the Impact of Event Scale-Revised and the Hopkins Symptom Checklist-25, respectively. The final manuscript presents a qualitative investigation of the meaning and experience of romantic betrayal among individuals with an adjustment disorder. Thirteen participants who completed the larger trial were interviewed using the McGill Illness Narrative Interview. Findings revealed that romantically betrayed individuals often use the trauma metaphors and prototypes to make sense of their experience with betrayal. Yet almost all participants did not identify their reaction as traumatic stress and were hesitant to use that idiom. However, framing the experience of betrayal as an emotional memory of the event, that can be attenuated, provided participants with a plausible framework for explaining their symptoms, as well as a treatment solution, which led to a sense of validation and relief. This thesis is the first to investigate the broader application of reconsolidation therapy to treat psychiatric disturbances rooted in a painful life-experience.

Abrégé

Un nombre grandissant d'écrits scientifiques suggèrent que certaines personnes trahies par un partenaire amoureux sont à risque de développer un trouble de l'adaptation (TA). Le TA est une condition psychiatrique classée dans la catégorie des troubles liés aux traumatismes et aux facteurs de stress caractérisée par des symptômes d'intrusions, d'évitement, et d'inadaptation. Cependant, il n'existe toujours pas de traitement efficace pour traiter le TA. Considérant que les troubles liés aux traumatismes et au stress sont ancrés dans les souvenirs émotionnels d'événements négatifs, réduire la valence émotionnelle d'un tel souvenir pourrait engendrer un effet thérapeutique. Des études précliniques montrent que l'administration du propranolol, un inhibiteur noradrénergique, avant la réactivation d'un souvenir émotionnel peut interférer avec sa reconsolidation, c'est-à-dire, avec la restabilization du souvenir en mémoire à long terme. Plusieurs études cliniques démontrent que cette approche, appelée la thérapie de la reconsolidation, est efficace pour réduire les symptômes de stress posttraumatique. Toutefois, aucune étude n'a été menée pour déterminer si cette thérapie pouvait également atténuer les symptômes liés à d'autres troubles de stress, tel que le TA. Les deux premiers manuscrits de cette thèse présentent le rationnel, la méthodologie et les résultats d'un essai clinique examinant l'efficacité de la thérapie de la reconsolidation pour le traitement du trouble de l'adaptation découlant d'une trahison amoureuse. Une série d'analyses de covariance (ANCOVA) révèlent que comparativement à la liste d'attente (n = 29), la thérapie de la reconsolidation (n = 30) entraîne une réduction significative des symptômes de stress, ainsi que la détresse psychologique. Ces derniers englobent les intrusions, l'évitement, et l'hypervigilance, ainsi que les symptômes anxieux et dépressifs, tel que mesuré au moyen de l'*Impact of Event Scale-Revised* et *la Hopkins Symptom Checklist-25*, respectivement. Le dernier manuscrit présente une enquête qualitative sur l'expérience de la trahison amoureuse chez les individus ayant un trouble de l'adaptation. Treize participants ayant complété l'essai clinique ont été interrogées à l'aide du *McGill Illness Narrative Interview*. Les résultats indiquent que les personnes trahies par un partenaire amoureux utilisent souvent des métaphores de trauma pour décrire leur expérience. Pourtant, les participants n'identifient pas leurs symptômes comme étant un stress traumatique, et semblent même réticents à employer cette terminologie. Néanmoins, présenter l'expérience de la trahison amoureuse un souvenir émotionnel de l'événement pouvant être affaibli a fourni aux participants un cadre plausible pour expliquer leurs symptômes, ainsi qu'une solution de

traitement, provoquant un sentiment de validation et de soulagement. Cette thèse est la première à proposer une application plus large de la thérapie de la reconsolidation pour tout trouble psychiatrique émanant d'une expérience de vie douloureuse.

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In November 2009 I began volunteering in Dr. Alain Brunet's laboratory on Psychological Trauma at the Douglas Research Center as an undergraduate student. Although I did not think too hard about where the work I was doing would lead, at the time I never thought that I would be completing a doctoral degree 10 years later. Now, after 5 years of blood, sweat, and tears, I am incredibly proud and honored to submit my PhD. Dissertation to McGill University's Department of Psychiatry in the Faculty of Medicine. Without question, there are a great number of people to whom I am eternally grateful, and without whom I would have never been able to complete this thesis.

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What a ride…

Contribution of Authors

This dissertation comprises a general introduction, an extended literature review, three manuscripts, and a general conclusion. The first two manuscripts present the methods and results of a clinical trial that was conceptualized and designed as a doctoral research project by myself and my supervisor, Dr. Alain Brunet (Chapter 3 and 4). The third manuscript (Chapter 5) presents a qualitative investigation that was designed by myself and Dr. Danielle Groleau, a qualitative research expert. My supervisor, Dr. Brunet, provided extensive guidance for the clinical trial, while Dr. Groleau is my co-supervisor responsible for supervising and conducting the qualitative study. Both contributed substantially to the design and execution of this project.

For the first manuscript, titled *Post-romantic stress disorder: Study protocol of a waitlist-controlled clinical trial involving reconsolidation therapy*, Dr. Alain Brunet and I conceptualized the methodology and wrote the manuscript. Dr. Monson co-wrote the initial draft and provided several rounds of revisions. Dr. Saumier, Sereena Pigeon, and Dr. Jaafari provided multiple rounds of revisions and edits throughout the initial and subsequent submission processes.

The second manuscript, titled *Eternal Sunshine of the Spotless Mind: A waitlist-controlled clinical trial of reconsolidation therapy to treat adjustment disorder following romantic betrayal*, was co-authored by myself, Daniel Saumier, Jacques Tremblay, Sereena Pigeon, Pierre Etienne, and Alain Brunet. Under the supervision of Dr. Brunet, I conducted psychological eligibility assessments and implemented the treatment protocol. I was also responsible for data collection, monitoring, analysis, and manuscript drafting. Dr. Saumier acted as a clinical and statistical consultant. Drs. Tremblay and Etienne were the clinical trial physicians. Sereena Pigeon was the primary research assistant on this project, who aided with data collection and monitoring, as well as participant evaluations and implementing the treatment protocol. All authors participated in editing and revising the manuscript.

For the third manuscript, titled *Is romantic partner betrayal a form of traumatic experience?* I designed the qualitative study with Dr. Danielle Groleau, who acted as the primary supervisor of this project and provided my training to conduct the qualitative interviews. With Dr. Groleau's supervision, I was responsible for data collection, monitoring, analysis, interpretation, and manuscript write-up. Marjolaine Rivest-Beauregard was the primary research assistant, participated in interview transcription, data monitoring, and data analysis. Dr. Groleau co-wrote the manuscript, and Dr. Brunet participated in multiple revisions and edits.

Statement of Original Contribution

- This research presents a novel contribution to the fields of event-related psychopathology and couple relationships. It has long been recognized that betrayal is an important factor in precipitating traumatic stress. However, little research has been conducted on forms of betrayal that may not meet the life-threat requirement of trauma, such as events perpetuated by romantic partners involving infidelity or sudden physical abandonment.

- Romantic partner betrayal can be experienced as a critical life event, which can precipitate symptoms similar to posttraumatic stress disorder, as well as depression, anxiety, and conduct disturbances. This syndrome may be best conceptualized as an adjustment disorder, an event-based stress-response syndrome characterized by symptoms of intrusions, avoidance, dysphoric mood and elevated anxiety, and functional impairment. The research comprised in this dissertation is the first to suggest romantic partner betrayal as a precipitating stressor, which has implications for future research examining the etiology and treatment of adjustment disorder.

- Intrusive memories of negative life events may underlie a range of psychopathology, including adjustment disorder. Reconsolidation therapy using propranolol is becoming an increasingly promising treatment for psychiatric disturbances rooted in dysregulated emotional memory mechanisms. However, most of the research on its clinical applicability has focused on individuals with PTSD, with a few studies examining either specific phobia or addiction. This is the first research study to propose and test the effectiveness of reconsolidation therapy using propranolol for adjustment disorder.

- This research also expands prior qualitative inquiries of the experience and meaning of romantic partner betrayal. Few studies have been conducted on the experience of romantic betrayal, and no research has examined whether the emotional memory framework of event-related distress is a plausible explanatory model of illness and treatment among relationally betrayed individuals.

Abbreviations

APA American Psychiatric Association

ANCOVA Analysis of Covariance

BTT Betrayal Trauma Theory

CAPS Clinician Administered PTSD Scale

CEQ Credibility / Expectancy Questionnaire

CGI-S Clinical Global Impressions – Severity scale

DSM *Diagnostic and Statistical Manual for Mental Disorders*

FCS Fully Conditional Specification

GPS Global Positioning System

HSCL-25 Hopkins Symptom Checklist-25

ICD-11 *International Classification of Diseases, Eleventh Revision*

IES or IES-R Impact of Event Scale or Impact of Event Scale-Revised

ITT Intention-to-treat analysis

MCAR Missing Completely at Random

MINI McGill Illness Narrative Interview

MINI-S Mini International Neuropsychiatric Interview-Simplified

PP Per Protocol analysis

PSS Posttraumatic Stress Disorder Symptom Scale

PTSD Posttraumatic stress disorder

SBQ-R Suicide Behaviors Questionnaire-Revised

WHO World Health Organization

WHOQOL-Bref World Health Organization Quality of Life-Bref scale

"Despite its widespread denunciation, infidelity has a tenacity that marriage can only envy."

- Esther Perel, Rethinking Infidelity: The State of Affairs

Chapter 1: Introduction

What if you could erase someone who deeply hurt you from your memory? Would you? This question inspired the 2004 film *Eternal Sunshine of the Spotless Mind,* which artfully illustrates the complexities of romantic relationships. Clementine and Joel are a young couple in love, yet after a particularly bad fight, Clementine impulsively decides that engaging in a procedure to erase all traces of Joel from her memory is the only way for her to move on; feeling betrayed and hurt by her actions, Joel does the same. The film highlights the unfortunate reality that while the behaviors of romantic partners can be the source of blissful contentment, they can also be the source of complete devastation. Although the film is the work of science-fiction, several of its themes are relevant to this dissertation: 1) the significance of romantic attachments to health and well-being; 2) the devastating effects of romantic partner betrayal; and 3) the importance of emotional memories to psychological health. This dissertation presents three manuscripts that aim to examine the experience, meaning, and treatment of the psychological distress that can stem from the discovery of romantic partner betrayal.

Romantic partner betrayal[1] is a common experience that is particularly damaging to individual and couple functioning and has far-reaching negative consequences for the couple's family and social network. Infidelity, for example, has been reported to occur in approximately 20% of marital relationships, with estimates being almost three times higher among those in non-marital dating relationships (Blow & Hartnett, 2005; Fincham & May, 2017; Maddox Shaw, Rhoades, Allen, Stanley, & Markman, 2013). Expanding the definition of betrayal to any act that is perceived to violate expectations of trust, loyalty, commitment, and exclusivity within a couple relationship (Johnson, Makinen, & Millikin, 2001), the prevalence of betrayal and its

[1] In this dissertation, romantic partner betrayal is defined as: An act that is perceived to violate relationship relevant norms and expectations of trust, loyalty, and commitment (Johnson et al., 2001).

consequences may be much greater. Betrayal events are the presenting problem for 29% to 65% of couple's seeking therapy, are especially difficult to overcome in treatment, and are among the top cited reasons for relationship dissolution (Scott, Rhoades, Stanley, Allen, & Markman, 2013; Whisman, Dixon, & Johnson, 1997). Experts have used theories of psychological trauma to contextualize the devastating effects of romantic betrayal for the injured individual, arguing that such events challenge implicit assumptions of safety and trust in the self, others, the world, and the future (Johnson et al., 2001). This assertion is eloquently illustrated by Dr. Dennis Ortman, who describes the experience of betrayal based on his clinical observations in a (2009) book entitled *Transcending Post-Infidelity Stress Disorder: The six stages of healing:*

> They [betrayed person] feel overwhelmed, enraged, and unable to cope with life. They are preoccupied with the betrayal, have nightmares about it, and suffer flashbacks. At times, they feel emotionally numb, then at other times, crazy. Their reaction can last for years and interferes with their capacity to enjoy life and trust others… [They] are often filled with rage, directing their anger, obviously, toward their partner, but also against themselves in self-blame. They also project their anger onto the world of relationships, which becomes dangerous and evokes mistrust (p. 3).

The diagnostic construct of adjustment disorder, categorized as a trauma-and stressor-related disorder in the 5th edition of the *Diagnostic and Statistical Manual for Mental Disorders* (*DSM-5*; American Psychiatric Association [APA], 2013), may be useful for understanding the psychological sequela of romantic betrayal. Adjustment disorder is a stress-response syndrome that, similar to posttraumatic stress disorder (PTSD), is characterized by event-related stress symptoms of intrusions / preoccupations, avoidance, and failure to adapt, as well as depression, anxiety, and functional impairment (Maercker, Einsle, & Köllner, 2007; Maercker & Lorenz,

2018). In contrast to PTSD, adjustment disorder can occur following a critical but non-life-threatening stressor, such as job loss or divorce. In addition to the humiliation and anger that follows the discovery of betrayal, specific symptoms experienced by injured persons may manifest as: denial, intrusive memories and re-experiencing the painful discovery process, persistent and uncontrollable thoughts and images about the context of the betrayal, increased vigilance or fear of experiencing betrayal again in the future, dysphoric mood / increased anxiety, and cognitive distortions surrounding safety and trust, all of which can be debilitating and enduring (Cano & O'Leary, 2000; Heintzelman, Murdock, Krycak, & Seay, 2014; Johnson et al., 2001; Kroger, Reisner, Vasterling, Schutz, & Kliem, 2012; Laaser, Putney, Bundick, Delmonico, & Griffin, 2017; Roos, Willetts, Canavello, & Bennett, 2017; Steffens & Rennie, 2006; Whisman, 2015). To date, there exists no intervention that has demonstrated consistent and reliable efficacy for adjustment disorder (see O'Donnell, Metcalf, Watson, Phelps, & Varker, 2018 for a review), and none directly targeted to the unique effects of betrayal.

One intervention that may prove beneficial stems from pathogenic memory models of event-related stress symptoms (Maercker & Lorenz, 2018; Marks, Franklin, & Zoellner, 2018; Pitman, 1989). It is well-demonstrated that activation of endogenous stress hormones (e.g., noradrenaline) within the amygdala during exposure to highly distressing or traumatic events potentiates memory consolidation (e.g., the transfer of information from short to long-term storage) and facilitates later recall (McGaugh, 2004). Reconsolidation theory posits that memory retrieval can trigger a transient period of lability and additional neurobiological processes that are required for memory persistence, recapitulating, at least in part, initial consolidation (Elsey, Van Ast, & Kindt, 2018). Administering the noradrenergic beta-blocker propranolol prior to retrieval dampens the enhancement of memory conferred by emotion, presumably by disrupting

memory reconsolidation (see Lonergan, Olivera-Figueroa, Pitman, & Brunet, 2013; Debiec & LeDoux, 2004). In clinical settings, this procedure, henceforth called reconsolidation therapy, has demonstrated success in reducing symptoms of PTSD (Brunet, Poundja, et al., 2011; Brunet et al., 2018), and other clinical syndromes based on pathological memory models (e.g., addiction, specific phobia; Lonergan et al., 2016; Soeter & Kindt, 2015). However, no research to date has investigated whether this approach may extend to stressor-related syndromes beyond PTSD, such as adjustment disorder. Further, there has been little investigation into the lived experience and meaning of romantic partner betrayal, which has limited treatment development.

The extended literature review (Chapter 2) presents the key elements necessary to not only consider romantic partner betrayal as a catalyst for adjustment disorder, but also propose reconsolidation therapy as a promising intervention. In Chapter 3, the first manuscript, entitled *Post-romantic stress disorder: Study protocol of a waitlist-controlled clinical trial involving reconsolidation therapy* and submitted for publication to *BMC Psychiatry*, disseminates the treatment protocol and proposes a research design to investigate the effectiveness of reconsolidation therapy. In Chapter 4, the results of this inquiry are presented in a manuscript in preparation for submission to the *Journal of Consulting and Clinical Psychology* entitled *Eternal Sunshine of the Spotless Mind: A waitlist-controlled clinical trial of reconsolidation therapy to treat adjustment disorder following romantic betrayal*. Finally, Chapter 5 consists of a manuscript entitled *Is romantic partner betrayal a form of traumatic experience?* in preparation for submission to the *Journal of Counseling Psychology*, which presents a qualitative investigation of the experience and meaning of romantic betrayal and its treatment from the perspective of the injured individual. The theoretical and clinical implications of these findings are discussed throughout the manuscripts and in the general conclusion (Chapter 6).

Chapter 2: Literature Review

"…if every person we met 'cut us dead', and acted as if we were non-existing things, a kind of rage and impotent despair would ere long well up in us, from which the cruellest bodily tortures would be a relief…" – William James, The Principles of Psychology, 1890

Overview

The three manuscripts presented in this dissertation rest on the assumption that adjustment disorder is the clinical expression of a pathogenic memory of a distressing life event (Maercker & Lorenz, 2018), and as such, can be effectively treated with a targeted memory-based approach. This review begins by defining trauma and delineating the trauma- and stressor-related disorders category of the *DSM-5* (APA, 2013). Next, an extensive search was conducted for studies exploring the nature and severity of the psychological consequences resulting from intimate partner betrayal; limitations of current treatments for the injured individual will be discussed. A theoretical framework based on psychological models of traumatic stress is presented to contextualize how romantic betrayal may be considered a critical life-event and precipitating stressor for adjustment disorder in the injured individual. This is followed by a discussion of the neurobiology of emotional memory and its role in the etiology, maintenance, and treatment of event-related pathology. A discussion of the evidence for a novel treatment for betrayal-related adjustment disorder that is congruent with memory reconsolidation will conclude this review.

Trauma- and Stressor-Related Disorders in the *DSM-5*.

Trauma-and stressor-related disorders are unique in the *DSM-5* in that they are the only category of psychiatric diagnoses that are temporally associated with an environmental etiological factor, e.g., the stressor. The *DSM-5* defines trauma under Criterion A. as direct or indirect exposure to actual or threatened death, serious injury, or sexual violence; repeated

indirect exposure to aversive details of horrific events through photographs or videos during the course of one's professional duties (e.g., detectives) also qualifies under the current definition (APA, 2013). Posttraumatic pathology following Criterion A. events can result in a diagnosis of acute stress disorder if symptoms resolve within one month or PTSD if symptoms persist for more than one month. Symptom criteria for PTSD (and acute stress disorder) are numerous and include: 1) intrusive thoughts, memories, and re-experiencing the event (e.g., nightmares); 2) avoidance of trauma-related cues and emotional numbing; 3) negative changes in cognitions and mood, such as excessive self-blame, guilt or anger, cognitive distortions surrounding safety and trust, feelings of estrangement, and anhedonia; 4) increased arousal and reactivity to contextual cues, emotional volatility, self-destructive behavior, hypervigilance, and difficulties with sleep and concentration; and 5) significant functional impairment (APA, 2013). Re-experiencing distressing aspects of the event through intrusive and uncontrollable thoughts, images, and memories has been considered the critical feature of traumatic stress from which other symptoms may stem (Iyadurai et al., 2018).

Recognizing that a range of negative life-events can precipitate a heterogeneous clinical presentation of stress-related pathology, adjustment disorder is a psychiatric disturbance recently reclassified as a trauma- and stressor-related disorder that can occur following a non-Criterion A. event (APA, 2013). The stressor typically represents a critical change in life's circumstances, and can be an acute event, such as divorce, job loss, or as argued here, romantic partner betrayal, or chronic in nature, such as living with increasing disability or persistent marital problems. Symptoms of adjustment disorder overlap with those of PTSD (e.g., intrusions or preoccupations with the stressor), as well as depression, generalized anxiety, and disturbance of conduct, and cause significant impairment in important areas of psychosocial function (Maercker et al., 2012;

Maercker & Lorenz, 2018). The *DSM-5* states that adjustment disorder is the appropriate diagnosis for individuals who meet the full symptom criteria for PTSD in response to a non-Criterion A. stressor, but who do not meet threshold for another disorder (e.g., major depressive episode). Conversely, adjustment disorder is also an appropriate diagnosis for individuals who meet some, but not all, of the PTSD diagnostic criteria following a Criterion A. event (e.g., sub-clinical PTSD; APA, 2013). Finally, the *DSM-5* specifies 6 subtypes of adjustment disorder: with 1) depressed mood, 2) anxiety, 3) mixed mood and anxiety, 4) conduct disturbance, 5) mixed emotional and conduct disturbance, or 6) unspecified. However, due to a lack of empirical evidence supporting the presence of distinctive subtypes, they have been removed from the formulation of adjustment disorder in the 11th edition of the *International Classification of Diseases* (*ICD-11*, World Health Organization [WHO], 2018; Maercker & Lorenz, 2018).

Adjustment disorder is very commonly diagnosed in primary care settings (Zelviene & Kazlauskas, 2018), with prevalence estimates ranging from 5% to 20% among outpatient mental health service users (APA, 2013). Although community-based prevalence rates are scarce, recent surveys indicate that approximately 1% to 2% of individuals will experience an adjustment disorder following a stressful life event (see Zelviene & Kazlauskas, 2018 for a review; Maercker et al., 2012). Per its definition, onset of adjustment disorder symptoms occurs within three months of the stressful event and persists for up to 6 months (APA, 2013). Symptoms lasting longer than 6 months once the stressor has terminated become classified under 'other specified trauma-and stressor-related disorders', or 'chronic adjustment disorder' if the stressor (or its consequences) persists (APA, 2013). While adjustment disorder is associated with decreased quality of life, and increased risk for suicide and progression into further

psychopathology, few empirically validated treatments exist to date (Casey, Jabbar, O'Leary, & Doherty, 2015; O'Donnell et al., 2018).

The Psychological Effects of Intimate Partner Betrayal

The association between intimate relationship distress and psychiatric disorders has been well-documented (Foran, Whisman, & Beach, 2015; Overbeek et al., 2006; Whisman, 2007). Although no research has directly investigated whether romantic partner betrayal can lead to an adjustment disorder in the injured individual, around the turn of the century, researchers became increasingly interested in investigating the role of specific negative relational events in precipitating psychiatric symptoms. For instance, Cano and O'Leary (2000) found that compared to women who did not experience a discrete marital stressor (e.g., infidelity, separation, financial deceit) within 2 months of study enrollment (n = 25), those who did (n = 25) were significantly more likely to be diagnosed with current major depressive episode (12% vs.72%, respectively), even when controlling for initial level of marital discord. Similar results were obtained by Christian-Herman, O'Leary, and Avery-Leaf (2001), where 67% of women with no history of mental health issues (n = 50) reported clinically significant depression 1 month following the discovery of betrayal; 33% continued to meet criteria 3 months later. More recently, after controlling for various demographic factors and baseline levels of marital satisfaction, Whisman (2015) found that discovery of infidelity was significantly and uniquely associated with past-year major depressive episode in the injured individual.

Increasingly, the emotional and behavioral reactions to relationship betrayals are being considered from a trauma perspective (Gordon, Baucom, & Snyder, 2004; Gordon, Khaddouma, Baucom, & Snyder, 2015; Johnson et al., 2001). Clinical observation reveals that romantically injured individuals often use trauma language, describing their experience with betrayal in life or

death terms (e.g., “I felt like I was drowning”; Pelling & Arvay-Buchanan, 2004; Johnson et al., 2001). Although scarce, qualitative investigations reveal that betrayal can be experienced as a shockingly unpredictable and overwhelming event that fundamentally alters an individuals’ sense of self, their view of their partner, and their trust in their current and future relationships (Haines, 2011; Klacsmann, 2008; Pelling & Arvay-Buchanan, 2004; Salavati, Mootabi, & Sadeghi, 2018; Zitzman & Butler, 2009). While such observations can be paralleled with several prominent psychological theories of trauma (see below; Brewin & Holmes, 2003; Horowitz, 1986; Janoff-Bulman, 1989), no study has investigated whether trauma theory is a plausible explanatory model of distress from the perspective of romantically injured individuals. Further, few empirical investigations have examined the extent to which romantic partner betrayal can result in ‘trauma-like’ event-related stress symptoms.

However, among the first to investigate this issue, Gordon et al. (2004) administered the Posttraumatic Stress Disorder Symptom Scale (PSS; Foa, Riggs, Dancu, & Rothbaum, 1993) to six couples participating in an infidelity-specific form of couple’s therapy within one year of discovery. At pre-treatment, injured individuals scored above the PSS’s cut-off of 15 (M = 21.0; SD = 12.4; Foa et al., 1993), indicating clinically significant event-related distress. In a randomized controlled trial of Gordon et al.’s (2004) intervention, Kroger, Reisner, Vasterling, Schutz, and Kliem (2012) extended these findings among 49 males and females injured by their spouse’s infidelity. At pre-treatment, scores on the Impact of Event Scale-Revised (IES-R; Weiss & Marmar, 1997) intrusion, avoidance, and hyperarousal subscales were comparable to what has been reported among trauma exposed substance dependent individuals suffering from PTSD (Rash, Coffey, Baschnagel, Drobes, & Saladin, 2008). Similar results were obtained by Steffens and Rennie (2006) in an examination of event-related stress symptoms among 63 women who

discovered their husbands were sexual addicts within two years of study entry. Finally, in a survey conducted by Heintzelman, Murdock, Krycak, and Seay (2014) of 587 couples where infidelity occurred at least 6 months prior to participation (*M* = 3.09 years; *SD* = 4.98), moderate levels of event-related distress were reported among injured individuals as measured by the IES (*M* = 36.72; *SD* = 4.21; Horowitz, Wilner, & Alvarez, 1979). Furthermore, time since the event was not a significant predictor of recovery, as measured by levels of posttraumatic growth.

Research published in several doctoral dissertations and presented at conference proceedings has also revealed clinically significant event-related stress symptoms following the discovery of infidelity. Özgün (2010) replicated findings by Gordon et al. (2004) in a sample of 182 married women; half of which had discovered infidelity between 7 months and 3 years prior to study entry, and a quarter reported betrayal occurring over 5 years prior. In this sample, severity of event-related stress symptoms, as measured by mean PSS scores, fell above the clinical cut-off (*M* = 19.23; *SD* = 7.76). Intrusion symptoms were particularly problematic for this sample, as demonstrated by mean scores on the re-experiencing subscale (*M* = 7.02; *SD* = 3.32) that were comparable to what has been reported among various trauma exposed individuals with and without PTSD (Foa, Cashman, Jaycox, & Perry, 1997). Finholt (2011) examined romantic betrayal more generally in an internet survey of 3,111 betrayed adults. Here, perceived severity of partner betrayal significantly predicted severity of event-related stress symptoms and depression. Further, the mean total severity score on the IES-R was 43.29 (*SD* = 18.55), 10 points higher than the widely accepted clinical cut-off of 33 (Creamer, Bell, & Failla, 2003). Such findings were more recently replicated by Roos et al. (2017), who examined the severity of event-related stress symptoms, depression, and anxiety in a sample of 59 undergraduates who had experienced infidelity within the previous 5 years; 51% of their sample scored above the

IES-R cut off (M = 49.83, SE = 2.40). These elevated scores were significantly correlated with severity of depression and anxiety, even when controlling for prior Criterion A. trauma exposure.

Other authors have investigated the frequency of event-related stress symptoms among romantically betrayed individuals. According to findings from Steffens and Rennie (2006), excluding the requirement for exposure to a life-threatening event (e.g., Criterion A.), close to 70% of women who had recently discovered their partner was chronically unfaithful (N = 47) met *DSM-IV-TR* symptom criteria for PTSD, as measured by the Posttraumatic Diagnostic Scale (PDS; Foa et al., 1997). Consistent with prior findings and anecdotal evidence (e.g., Glass, 2002; Ortman, 2005), intrusion symptoms were the most frequently reported in this sample. Although up to 75% of participants had experienced prior interpersonal trauma (e.g., assault), suggesting a high-risk sample, there was no difference in symptom severity between women with past trauma exposure and those without. However, the number of previous traumatic experiences was significantly predictive of symptom severity. Others, perhaps counterintuitively, have included Criterion A. in their diagnostic assessment. For instance, Laaser, Putney, Bundick, Delmonico, and Griffin (2017) surveyed 202 women relationally betrayed by a current romantic partner. According to findings from these authors, 61% of the sample met all *DSM-5* PTSD criteria.

Several limitations of the literature reviewed above should be noted, including generalizability issues (e.g., a majority of participants consisted of heterosexual Caucasian women), retrospective assessment of symptom severity and diagnosis using self-report measures, inconsistency in the measurement and operationalization of betrayal, and limited attempts to clinically and statistically control for confounding factors, such as comorbid psychopathology or lifetime history of trauma exposure. For instance, Laaser et al. (2017) did not describe the context of the betrayal events and asserted that participants met Criterion A. for PTSD based on

their operational definition of betrayal as involving 'repeated or extreme exposure to aversive details of the traumatic event' (APA, 2013). However, this interpretation of Criterion A. may have been inaccurate, as traumatic events are *required* to involve either direct or indirect exposure to life-threat (APA, 2013). Without knowing the context of the betrayal events, it is uncertain whether this condition was met, as betrayals that do not involve life-threat would not meet threshold for PTSD diagnosis. Additionally, given that the prevalence of PTSD among Criterion A. trauma exposed individuals is slightly less than 10% (Kilpatrick et al., 2013), the diagnostic estimates found by these researchers seem quite high, which possibly reflects an upward bias obtained from the use of self-report symptom measures.

In sum, the extent to which romantic partner betrayal directly causes a diagnosable psychiatric disorder (e.g., trauma- or stressor-related disorder or depression), or whether the trauma framework is a plausible explanatory model of symptoms from the perspective of the injured individual, is uncertain. Nevertheless, taken together, the evidence reviewed here suggests that intimate partner betrayal may precipitate enduring event-related stress symptoms, including intrusions, avoidance, increased vigilance, and cognitive distortions among others, as well as clinically significant depression and anxiety in the injured individual. As discussed further below, such a syndrome is largely reflective of the core clinical characteristics of adjustment disorder, particularly as conceptualized by Maercker et al. (2007).

Current Treatments for Adjustment Disorder and the Relationally Betrayed Partner

It is within the context of the couple's therapy literature that the effects of romantic partner betrayal have been most obviously conceptualized within trauma theory (e.g., Gordon et al., 2004; Makinen & Johnson, 2006). Gordon et al. (2004) developed an infidelity specific treatment based on their forgiveness model, which parallels recovery from relational betrayals

with recovery from trauma paradigms emphasizing restoration of safety and trust. This approach has been investigated in several small studies, which have shown some promise, particularly for reducing event-related stress symptoms and marital distress in the injured individual, although the effects of the intervention on depression have been mixed (Gordon et al., 2004; Kroger et al., 2012). Other teams have examined the efficacy of augmented versions of Emotion Focused Couples' therapy, the most empirically-validated dyadic intervention, designed to directly target relational betrayals (Greenberg, Warwar, & Malcolm, 2010; Halchuk, Makinen, & Johnson, 2010; Makinen & Johnson, 2006). Although results of such studies are encouraging, these approaches have only been investigated among treatment-seeking couples, where both parties are involved in the therapeutic process. Many individuals affected by betrayal may not stay in the relationship long enough to enter couple's therapy (Adamopoulou, 2013; Allen & Atkins, 2012). Marriages with a history of infidelity, for example, are 2 to 4 times more likely to end in divorce (Allen & Atkins, 2012), and these rates may be even higher within non-married dating or cohabitating relationships (Adamopoulou, 2013). While the principles and therapeutic steps involved in these dyadic approaches may be successfully translated to individual psychotherapy, this has yet to be empirically examined.

Some individuals suffering a possible adjustment disorder in the aftermath of betrayal may seek individual counseling to cope with their suffering. Epidemiological surveys reveal that after controlling for mood, anxiety, and substance used disorders, intimate relationship distress is among the primary predictors of use of mental health services (Foran et al., 2015; Schonbrun & Whisman, 2010). While psychotherapy, including cognitive-behavioral approaches, is the recommended intervention for adjustment disorder and can be beneficial for some, efficacy evidence is limited and there is no scientific consensus regarding which form of psychotherapy is

optimally suited for adjustment disorder (Casey, 2014; O'Donnell et al., 2018). Furthermore, psychotherapy is costly in both time and money, and not always readily available in primary care settings where most adjustment disorder diagnoses are made (Casey, 2014).

Conversely, other suffering individuals may be prescribed antidepressants to cope with their distress. In indirect support of this notion, a large Finnish epidemiological survey revealed that use of antidepressants sharply increases within the year prior to divorce, and although declines slightly in the two years post-divorce, continues to be more prevalent among divorced compared to continuously married individuals (Metsä-Simola & Martikainen, 2013). Such pharmacological options are typically recommended in cases where psychotherapeutic approaches have been unsuccessful (Casey, 2014; Zelviene & Kazlauskas, 2018). However, a community survey of United States residents revealed that the number of psychotropic prescriptions for adjustment disorder almost doubled between 1996 and 2005, and this was combined with a decline in the number of pharmacologically-treated individuals engaging in psychotherapy (Olfson & Marcus, 2009). Interestingly, these trends occurred against the backdrop of limited evidence for the efficacy of pharmacotherapy for adjustment disorder (O'Donnell et al., 2018).

In sum, the available evidence for effective treatments for adjustment disorder is limited (O'Donnell et al., 2018). Further, there exists no research to date on manualized individual treatments for the effects of romantic partner betrayal, despite increasing recognition of its devastating effects and the subsequent development of trauma-informed dyadic interventions. Such findings call to attention the necessity for further investigations into the treatment of adjustment disorder more generally, and betrayal-related adjustment disorder more specifically.

Etiology of Event-Related Stress: Shattered Assumptions and Emotional Memory

Intrusive thoughts, images, and memories of distressing life experiences are not only a main clinical feature of trauma-and stressor-related disorders, but also associated with a range of mental health conditions (e.g., depression), rendering them a vital target for clinical and academic attention (Lipton, Brewin, Linke, & Halperin, 2010; Maercker & Lorenz, 2018; Mihailova & Jobson, 2018; O'Toole, Watson, Rosenberg, & Berntsen, 2016; Marks et al., 2018). While learning models point to the role of conditioning and memory in the etiology of event-related distress (see below), to account for individual differences and clinical heterogeneity, cognitive theories emphasize the importance of the subjective meaning of the stressor (e.g., Ehlers & Clark, 2000; Brewin & Holmes, 2003). Negative appraisals about the cause and consequences of the event can promote cognitive distortions surrounding safety and trust, leading to an enduring sense of threat (Ehlers & Clark, 2000). According to these models, core event-related stress symptoms arise following experiences that shatter previously held beliefs in the self as competent and capable, others as trustworthy, and the world as safe, predictable, and controllable, or conversely, when such experiences confirm prior negative worldviews (Ehlers & Clark, 2000; Foa et al., 1989; Janoff-Bulman, 1989). In short, the persistence of stressor-related pathology is argued to involve pre-existing vulnerability factors, combined with dysregulated or maladaptive neurobiological and cognitive processes that occur during and after event-exposure (Brewin et al., 2010; Marks et al., 2018; Maercker & Lorenz, 2018).

Similar to Horowitz's (1986) early conceptualizations, Maercker et al. (2007) draw from these theoretical models to propose adjustment disorder as a stress-response syndrome predominantly characterized by intrusions, avoidance, and failure to adapt. According to Maercker et al. (2007), although the precipitating stressor is of lesser intensity in adjustment

disorder than PTSD (e.g., does not involve threat of death or serious bodily harm), the etiology, psychological experience of the event, and resulting symptoms are similar (see also Maercker & Lorenz, 2018). Further, adjustment disorder can be distinguished from a normal stress reaction to a negative life event based on the severity and duration of symptoms and impairment (Maercker & Lorenz, 2018; Zelviene & Kazlauskas, 2018). This model has received increasing empirical support (e.g., Glaesmer, Romppel, Brähler, Hinz, & Maercker, 2015; Maercker et al., 2012), prompting the reformulation of adjustment disorder in the *ICD-11* (WHO, 2018). Perhaps most importantly, this work has put forth a number of testable hypotheses for future neurobiological and psychological research aimed at further clarifying the etiology of adjustment disorder, which has important treatment implications.

Since human-generated negative events appear to be particularly threat-inducing, the role of trust and betrayal has long been discussed in the trauma literature (Anders, Frazier, & Frankfurt, 2011; Anders, Shallcross, & Frazier, 2012; Brothers, 1995; Charuvastra & Cloitre, 2008). For example, betrayal trauma theory (BTT) suggests that the level of betrayal involved in an interpersonally negative event will vary as a function of the attachment significance of the relationship (e.g., the level of closeness between offender and offended), which in turn, will influence the way the event is cognitively processed and subsequently, clinically expressed (Freyd, 1996; Freyd, DePrince, & Gleaves, 2007). Although BTT is most often studied in the context of interpersonal trauma (e.g., childhood / domestic abuse), Johnson et al. (2001) put forth the notion of attachment injury to describe a specific form of betrayal ‘trauma’ that can occur when one partner violates the expectation of trust, loyalty, commitment, and safety within a romantic relationship. Both the construct of attachment injury and BTT have roots in attachment theory, the most prominent framework for understanding adult love relationships (Hazan &

Shaver, 1987). Attachment theory emphasizes the innate human motivation to form strong and secure bonds with primary attachment figures (e.g., parents, romantic partners) throughout the lifespan, and conversely, the detrimental effects of betrayal or abandonment by such caregivers (Bowlby, 1969, 1973, 1980). As Johnson et al. (2001) suggest, romantic partner betrayal, or attachment injuries, may be best understood as "trauma with a small 't'" (p. 150), considering that such events likely do not involve imminent life-threat. Together, these theories propose that similar to trauma, acts of betrayal challenge fundamental assumptions about the self, others, and the world. As a result, such experiences may precipitate a clinical syndrome that is ingrained in the subjective meaning and emotional memory of the distressing life experience, such as adjustment disorder (Freyd et al., 2007; Johnson et al., 2001; Maercker & Lorenz, 2018).

The neurobiology of emotional memory: A role for love and betrayal. Emotional experiences are remarkably well-remembered. While the hippocampus is involved in declarative memory consolidation, activation of the noradrenergic system within the amygdala during exposure to emotional stimuli potentiates this process (McGaugh, 2004, 2013). In human pre-clinical studies, administering adrenergic agonists prior to learning strengthens memory for emotional material and facilitates later recall (O'Carroll, Drysdale, Cahill, Shajahan, Ebmeier, 1999a), while the adrenergic antagonist propranolol impairs consolidation and inhibits emotional memory enhancement (Cahill, Prins, Weber, & McGaugh, 1994; McGaugh, 2013). Once thought to be permanent and static, it is now understood that under certain conditions, the reactivation (i.e., retrieval) of long-term emotional memories induces a transient period of lability in a process of neuroplasticity referred to as memory reconsolidation (see Elsey et al., 2018 for a review). As in memory consolidation, the reconsolidation of emotional material involves (re)activation of the noradrenergic system within the amygdala, among other processes including

de novo protein synthesis (Dębiec & Ledoux, 2004; Nader, Schafe, & Le Doux, 2000; Przybyslawski, Roullet, & Sara, 1999; Tully & Bolshakov, 2010). It is argued that reconsolidation mechanisms serve to strengthen, weaken, or otherwise update long-term memories, particularly when presented with new and pertinent information (Lee et al., 2017; Tronson & Taylor, 2007).

Human emotional memory likely serves an evolutionary purpose, allowing individuals to learn and 're-learn' which experiences to pursue again in the future, which to avoid, and of relevance here, *who* to pursue or avoid in the future (Eisenberger & Cole, 2012; Lee, Nader, & Schiller, 2017; McGaugh, 2004, 2013). However, for some individuals, the underlying neurobiological mechanisms of emotional memory may be dysregulated. Indeed, etiological learning models of event-related stress symptoms propose that exposure to a distressing or traumatic event prolongs the stress response, resulting in an 'overly' consolidated pathogenic memory that is too easily activated. Subsequent re-exposure to event-related cues provokes heightened conditioned emotional and behavioral responses in the form of intrusions, re-experiencing, and hypervigilance, while avoidance and emotional numbing maintain the pathology through negative reinforcement (Marks et al., 2018; Brewin, Gregory, Lipton, & Burgess, 2010; Foa, Steketee, & Rothbaum, 1989; Pitman, 1989). Thus, while the salience of emotional memories dissipates with time for most, persistent hypermnesia of an emotional event through repeated and distressing cued and involuntary retrievals may underlie core stressor-related pathology (see Marks et al., 2018).

The amygdala is responsible for modulating the consolidation and expression of a variety of emotional stimuli, including fear / threat- and reward-related learning (McGaugh, 2004, 2013; Tronson & Taylor, 2007). Relevant to the current discussion, fMRI studies of individuals either

happily in love, or still in love with a rejecting partner, have revealed activation in brain regions, including the ventral tegmental area, caudate nucleus, nucleus accumbens, and orbitofrontal cortex, when presented with photographs of the lover (or rejector; Aron et al., 2005; Fisher, Aron, & Brown, 2005; Fisher, Brown, Aron, Strong, & Mashek, 2010). Such activations were not observed when participants were presented with neutral photographs consisting of familiar individuals who approximated the physicality of the lover or offender. Together with the hippocampus and amygdala, these brain areas are part of the mesolimbic dopaminergic reward system, which is implicated in the pathophysiology of craving in addiction, also argued to be rooted in dysfunctional emotional memory mechanisms (Torregrossa, Corlett, & Taylor, 2011). Thus, as Fisher et al. (2010) argue, romantic love is more than a feeling; love is an innate motivational state that has evolved as a function of survival needs (see also Aron et al., 2005).

Strong social networks play a crucial role in buffering the negative physical and psychological effects of adversity and more generally, promoting the survival of our species (Charuvastra & Cloitre, 2008; Eisenberger & Cole, 2012). Hence, it is no surprise that social injuries are painfully experienced. Among romantically rejected participants in Fisher et al.'s (2010) study, activations were also found in brain areas involved in the experience of physical distress when presented with reminders of the rejector, such as the insular cortex, suggesting common neural pathways between romantic and physical pain. Several other studies in healthy populations have demonstrated that compared to the experience of physical injury, social injury (e.g., betrayal by someone close) was more easily and painfully re-lived (see Chen & Williams, 2011 for a review; Chen, Williams, Fitness, & Newton, 2008). Thus, some argue that the threat of social injury recruits neural 'alarm' circuits that overlap with those involved in the threat of physical injury (Eisenberger & Cole, 2012). For instance, in an experimental paradigm of social

deception, Grezes, Berthoz, and Passingham (2006) found significant increases in amygdala activation when one was personally deceived, compared to witnessing another being deceived, highlighting the personal significance of social threat. Arguably, betrayal events represent a critical psychological threat to the sense of safety and the social attachment system, and as such, the pain of betrayal and rejection may be processed by the neurobiological interaction between emotion and memory (Eisenberger & Cole, 2012).

Relationship experts have long asserted that for certain individuals, the experience of betrayal leaves an 'indelible imprint' of the event that is constantly re-experienced in the form of distressing thoughts, images, and memories (Horowitz, 1986; Johnson et al., 2001). Preliminary neurobiological evidence suggests that this may be the case. However, this line of inquiry is still in its infancy and the evidence has not always been consistent (Cacioppo et al., 2013). Nevertheless, considering pathogenic and intrusive memories of a range of distressing life events as a transdiagnostic and clinically important phenomenon (Marks et al., 2018; Maercker & Lorenz, 2018), it is possible that an 'overly consolidated' emotional memory of the betrayal event underlies, at least in part, the resulting pathology.

Disrupting memory reconsolidation: Pre-clinical evidence. Memory reconsolidation theory was first proposed in the 1960's and 1970's, after it was revealed that administering electroconvulsive shocks or hypothermia shortly after the retrieval of a consolidated fear memory abolished the behavioral expression of fear in rodents (Mactutus, Riccio, & Ferek, 1979; Misanin, Miller, & Lewis, 1968). However, it was not until the late 1990's that it was discovered that an adrenergic receptor blocker known to inhibit emotional memory consolidation, propranolol, also interfered with emotional memory re-stabilization following retrieval (Przybyslawski et al., 1999). Since then, there has been an explosion of experimental research

aimed at investigating the molecular, cellular, and structural correlates, as well as clinical applications, of memory reconsolidation (Besnard, Caboche, & Laroche, 2012; Ecker, 2018; Elsey et al., 2018). In human experimental settings, the typical research protocol to investigate reconsolidation is a three-stage process: 1) participants engage in a learning or behavioral conditioning task, usually involving emotional vs. neutral material (e.g., word lists, pictures, conditioned stimuli); 2) at least 24-hours later, the memory is reactivated by a brief presentation of the learned or conditioned stimulus either before (60-90 minutes) or immediately after administration of propranolol or placebo; and 3) again at least 24-hours later, participants' memory is tested via recall or recognition tasks, or by physiological reactivity to the conditioned stimulus (Elsey et al., 2018).

Propranolol hydrochloride is a lipophilic beta-1 and beta-2 adrenergic receptor blocker that crosses the blood-brain barrier, exerting central as well as peripheral inhibitory effects on the nervous system (O'Carroll, Drysdale, Cahill, Shajahan, & Ebmeier, 1999b). It is commonly prescribed to treat hypertension, migraines, and other cardiovascular ailments, and because of its anxiolytic properties, it is also used off-label for anxiety states such as stage fright (Dooley, 2015). Among other brain areas, beta-adrenergic receptors are found in both the amygdala and hippocampus and are coupled with the cyclic adenosine monophosphate (cAMP) / protein kinase A (PKA) cascade involved in *de novo* protein synthesis that is necessary for late long-term potentiation (i.e., the strengthening of synapses), which underlies memory consolidation and (at least partly) reconsolidation (Huang & Kandel, 2007; Nader et al., 2000; Schafe & LeDoux, 2000). Although the complexities of the precise mechanisms require much more clarification, one possibility is that propranolol reduces or blocks noradrenergic activity within the amygdala, which may indirectly interfere with the synthesis of new proteins by disrupting the cAMP/PKA

pathway, and subsequently, the (re)consolidation of emotional memories (Huang & Kandel, 2007; Hurlemann et al., 2010; Tully & Bolshakov, 2010).

Employing the experimental paradigm described above, a meta-analysis of studies investigating reconsolidation impairment of emotionally aversive stimuli in healthy populations revealed a moderate effect size of $g = .56$ in favor of propranolol compared to placebo (Lonergan et al., 2013). Importantly, there were no significant differences between studies that employed declarative emotional memory tasks (e.g., word lists or pictures; $g = .58$), or conditioning paradigms (e.g., psychophysiological reactivity; $g = .57$). Some studies have also demonstrated that propranolol induced reconsolidation impairment selectively blunts the emotional tone of the memory. For instance, Soeter and Kindt (2010) found that compared to placebo, pre-reactivation propranolol led to a significant reduction in startle response to a fear-conditioned stimulus, while no effects were observed on declarative associative memory. Such findings have been extended to reward-related or appetitive memories, such as those underlying drug craving and relapse in substance dependence (Cogan, Shapses, Robinson, & Tronson, 2018). This line of inquiry has important implications for any ethical concerns raised by the perception of reconsolidation impairment using propranolol as a memory 'erasure' process (e.g., McGorrery, 2017; but see Elsey & Kindt, 2018). As suggested by these findings, disrupting emotional memory reconsolidation may its emotional salience, but factual or declarative knowledge remains unaffected. It may be useful to conceptualize this process as mimicking the natural conditions under which emotional memories diminish over time.

Clinical applications of reconsolidation theory. Based on conditioning models of psychopathology, extinction-based therapies (e.g., exposure therapy) are among the most empirically-based interventions for a variety of fear-based or stressor-related disorders (e.g.,

PTSD, social phobia, specific phobia, obsessive compulsive disorder; Carl et al., 2018; Foa & McLean, 2016; Kaczkurkin & Foa, 2015). These approaches involve repeated exposure to the stressor or anxiety provoking stimuli until the conditioned behavior subsides. However, because extinction-based interventions result in the consolidation of a new memory that competes with the original trace during retrieval, such therapies are vulnerable to three phenomena which limit confidence in their long-term efficacy: 1) reinstatement (i.e., the return of a conditioned response following the unexpected presentation of an environmental cue), 2) spontaneous recovery (i.e., the return of a conditioned response after time), and/ or 3) renewal (i.e., the return of a conditioned response in a context other than the one used for extinction or associated with the trauma; Beckers & Kindt, 2017; Bradley, Greene, Russ, Dutra, & Westen, 2005). What's more, exposure-based therapies have seldom been directly explored in the treatment of adjustment disorder, rendering their efficacy in such cases virtually unknown (O'Donnell et al., 2018). Conversely, since disrupting reconsolidation directly targets and modifies the original pathological memory trace, it is not vulnerable to the effects of recovery, reinstatement, or renewal (Beckers & Kindt, 2017). Thus, over the last 15 years, the clinical application of disrupting memory reconsolidation, or reconsolidation therapy, has been gaining increasing attention from a range of academic and clinical communities.

In one of the first pilot investigations, Brunet et al. (2008) administered, in a double-blind manner, propranolol (n = 9) or placebo (n = 10) to patients with chronic PTSD immediately after memory reactivation, which was achieved by having participants write a detailed narrative of the traumatic event. One-week later, participants engaged in a script-driven imagery task, where they listened to their personal trauma narrative while psychophysiological measurements (e.g., heart rate, skin conductance, left corrugator electromyogram) were recorded; these outcomes represent

an objective biological measure of traumatic stress (Orr & Roth, 2000). Results revealed a significant attenuation of psychophysiological arousal to trauma narratives only in the propranolol condition. A later open-label trial involving 22 patients with chronic PTSD, who received 6-weekly reconsolidation therapy sessions, demonstrated that reduced physiological arousal to trauma narratives was maintained at a 4-month follow-up (Brunet et al., 2014). Since then, disrupting memory reconsolidation using propranolol has been shown to reduce behavioral responses to fear among individuals with spider phobia (Soeter & Kindt, 2015), traumatic stress symptoms in PTSD patients (Brunet et al., 2018), and craving in addiction (Lonergan et al., 2016), demonstrating its potential as a promising therapeutic approach.

An important caveat to consider when evaluating the strength of the evidence from reconsolidation studies is the timing of study drug administration. A large number of pre-clinical and clinical studies employ *pre*-reactivation propranolol, which some argue cannot rule out the possibility that the observed results are due to propranolol's effects on memory retrieval rather than reconsolidation (Schiller & Phelps, 2011; but see Brunet, Ashbaugh, et al., 2011). To address this issue, propranolol should ideally be given *post*-reactivation; however, findings from such studies are more inconsistent (Lonergan et al., 2013; Thomas, Saumier, Pitman, Tremblay, & Brunet, 2017). The reconsolidation window begins within 3-10 minutes following reactivation and is most active for approximately 2 hours before completing within 6 hours (Duvarci & Nader, 2004; Monfils, Cowansage, Klann, & LeDoux, 2009). Despite findings from Brunet et al. (2008), post-reactivation drug administration may be more likely to provide negative results, as this window may have closed by the time propranolol has reached its peak bioavailability in the brain, which occurs within 1-2 hours (Brunet, Ashbaugh, et al., 2011; Dey et al., 1986; Elsey et al., 2018). One recent investigation provides indirect support for this notion, where propranolol

administered 60-75 minutes before reactivation reduced memory for an emotional slide story, while immediate post-retrieval propranolol had no effect on memory performance (Thomas et al., 2017). Further, in a double-blind placebo-controlled experiment, Schwabe, Nader, Wolf, Beaudry, and Pruessner (2012) found no effect of propranolol on memory retrieval when examining amygdala activity via fMRI, although a significant reduction in memory for emotional pictures was observed, suggesting that propranolol interfered with reconsolidation.

Therefore, the treatment protocol for reconsolidation therapy that has been subsequently developed and investigated among patients with PTSD involves drug administration at least 60-75 minutes prior to having participants write (session 1) and read aloud (sessions 1 to 6) a detailed narrative of the traumatic experience in the 1st person, present tense (Brunet & Lonergan, manual in preparation; Brunet, Poundja, et al., 2011; Brunet et al. 2018). Each writing and / or reading exercise (one per week for up to 6 weeks) serves to reactivate the memory, and are purposefully kept brief (e.g., 10-25 minutes) to minimize extinction effects (Tronson & Taylor, 2007). To account for individual differences in the metabolism of propranolol, drug dosage is typically set at 1mg/kg of body weight, although this is capped depending on a persons' body mass index given that propranolol is metabolized in muscle tissue (Cheymol et al., 1997). The inclusion of six-weekly sessions was initially chosen somewhat arbitrarily; anecdotally, treatment effects have been observed as early as the fourth visit, suggesting that the number of sessions required for successful symptom reduction may vary as a function of the condition under study or the individual patient.

Using this treatment protocol, Brunet, Poundja, et al. (2011) demonstrated, in three open-label trials, a significant reduction in PTSD symptoms and diagnosis at post-treatment that was maintained, in one study, for up to 6-months. Given that it is not possible to tease out 'placebo'

effects via open-label trials with no controls, these results were recently extended in a double-blind randomized controlled trial (Brunet et al., 2018). In both an intention-to-treat (e.g., retaining all randomized participants regardless of whether they completed the trial), and a per protocol analysis (e.g., retaining only those who completed and did not significantly deviate from the treatment or research protocols), results revealed that clinician-rated and self-report PTSD symptoms were significantly reduced in propranolol treated participants (n = 30), relative to placebo participants (n = 30), at post-treatment. In the intention-to-treat analysis, the pre-post effect size for self-report symptoms, as measured with the PTSD Checklist (Weathers, Litz, Herman, Huska, & Keane, 1993), was very large (d = 2.74) for propranolol treated participants and moderate (d = .55) for placebo participants. Further, clinician-rated percent improvement, as measured with the Clinician Administered PTSD scale (Blake et al., 1995), was 38% in the propranolol group, compared to 24% in the placebo group. Although participant attrition precluded more thorough statistical analyses of follow-up data, this study represents the first large scale placebo-controlled clinical trial demonstrating the clinical efficacy of reconsolidation therapy for chronic PTSD.

Notably, sustained effects of propranolol induced reconsolidation impairment in clinical settings have not always been obtained (Pachas et al., 2015; Saladin et al., 2013; Wood et al., 2015). In addition to between-study methodological differences, another possible reason for this may stem from so-called ‘boundary conditions’ on reconsolidation (Lee et al., 2017). For instance, Beckers and Kindt (2017) argue that if reconsolidation serves as a memory updating mechanism, then there must be some new and pertinent information that needs to be integrated into the original trace; retrieval alone is insufficient, as it would not be adaptive for a memory to enter a lability phase each and every time it is remembered. This opinion has been echoed by

others (Agren, 2014; Ecker, 2015; Lee et al., 2017), who, based on findings from pre-clinical evidence (e.g., Alfei, Monti, Molina, Bueno, & Urcelay, 2015), suggest that a certain degree of 'mismatch', or prediction error, between the original memory and new information must be present in order for a memory to destabilize and enter the reconsolidation phase following retrieval. It can be argued that in clinical studies with successful results, some level of mismatch was introduced in addition to retrieval (e.g., writing vs. reading a narrative), which was sufficient to trigger deconsolidation and the subsequent impairment of reconsolidation with propranolol (Agren, 2014; Ecker, 2015). However, the mismatch phenomenon has yet to be carefully and explicitly investigated in clinical applications of reconsolidation. Nevertheless, this approach has the potential to treat a range of disturbances either stemming or complicated by pathogenic emotional memories (Ecker, 2018).

Summary and Objectives of Dissertation

Similar to psychological trauma, romantic partner betrayal can cause seemingly irreparable damage to fundamental assumptions about the self and the partner, as well as of current and future intimate relationships (Janoff-Bulman, 1989; Johnson et al., 2001; Laaser et al., 2017). Indeed, intrusive thoughts, images, and memories of such highly distressing life events have been considered a transdiagnostic clinical phenomenon that may drive other event-related stress symptoms, such as avoidance, increased vigilance, depression, and anxiety (Iyadurai et al., 2018; Marks et al., 2018). Although it does not incorporate the construct of betrayal in its definition of stressors, the *DSM-5* recognizes the role of non-life-threatening yet critical events in the etiology of psychopathology with its diagnostic construct of adjustment disorder (APA, 2013; Maercker & Lorenz, 2018). In this dissertation, romantic partner betrayal is conceptualized from a 'trauma' perspective, but not to equate the experience of betrayal with

that of Criterion A. life-threatening events leading to PTSD. Rather, a parallel is drawn based on mounting empirical evidence suggesting that romantic partner betrayal can precipitate event-related stress symptoms in some injured individuals, which is argued here to be more reflective of adjustment disorder (Laaser et al., 2017; Maercker & Lorenz, 2018; Roos et al., 2017).

Considering that pathogenic emotional memories of negative life events may underlie a range of disturbances (Maercker & Lorenz, 2018; Marks et al., 2018), decreasing their emotional strength by pharmacologically disrupting memory reconsolidation would likely produce a desirable outcome. To date, however, no study has investigated whether reconsolidation therapy using propranolol can reduce event-related stress symptoms stemming from the discovery of romantic betrayal. Furthermore, while results from qualitative inquiries examining the experience and meaning of romantic betrayal have been interpreted in light of trauma theory (Pelling & Arvay-Buchanan, 2004; Zitzman & Butler, 2009), no research has investigated whether this framework is a plausible explanatory model of symptoms from the perspective of injured individuals. The objective of the research presented in this dissertation is to address these two knowledge gaps. Such inquiries will make substantial contributions to understanding and treating the effects of romantic partner betrayal.

The following manuscript (Chapter 3) disseminates the treatment and research protocols for investigating reconsolidation therapy, which has extensive implications for researchers aiming to further investigate this intervention in various clinical populations, as well as clinicians wishing to incorporate it into their practice. The results of this clinical trial are presented in Chapter 4. Finally, Chapter 5 presents a qualitative investigation examining the experience and meaning of romantic partner betrayal. The implications of this research are discussed throughout the manuscripts and in the general conclusion, Chapter 6.

Chapter 3

Post-romantic stress disorder: Study protocol of a waitlist-controlled clinical trial involving reconsolidation therapy

"When you run into something interesting, drop everything else and study it".

– B.F. Skinner, A Case History in Scientific Method

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Abstract

Background*:* Romantic partner betrayal can precipitate an adjustment disorder in the injured partner, which is classified in the trauma- and stressor-related disorders in the *DSM-5*. To date, manualized treatment approaches for this condition are scarce. **Objective***:* To describe the methodology of a clinical trial using reconsolidation therapy to treat betrayal-related adjustment disorders. **Methods*:*** This study will compare a waitlist group (n = 30) to a treatment group (n = 30) receiving four to six 10-25minute sessions of reconsolidation therapy using on severity of adjustment disorder symptoms at post-assessment and 3-month follow-up. The primary hypothesis predicts a significant effect of treatment for reducing event-related stress symptoms on the patient-rated Impact of Event Scale-Revised in an intention-to-treat analysis. This study has received approval from all relevant ethics and regulatory authorities. **Discussion*:*** This trial will explore the usefulness of reconsolidation therapy beyond the treatment of traumatic stress, as a treatment modality for disorders stemming more generally from a negative life-event. **Trial registration:** Clinicaltrials.gov NCT03151681 retrospectively registered on April 29, 2017

Keywords: Romantic betrayal, Reconsolidation, Memory, Adjustment Disorder, Randomized trial.

Background

A positive and secure romantic attachment is associated with health, well-being, and longevity [1]. But when this attachment bond is threatened by the deceptive actions of one partner, the results can be devastating. This is well illustrated by the most frequently performed Greek tragedy throughout the 20th century [2], Euripides' *Medea*, who attempts to murder her partner after being abruptly betrayed and abandoned.

Betrayal of trust is among the most frequently cited reasons for couple separation and is notably difficult to treat in couple's therapy [3]. Experts suggest that the earth-shattering nature of betrayal –not unlike traumatic stress– challenges our most basic assumptions of safety and trust in the self, in others, and the world [3-5]. The profound feelings of powerlessness, vulnerability, abandonment, and rage that can occur following the discovery of betrayal may lead to an adjustment disorder in the injured partner, a psychiatric disturbance characterized by symptoms of anxiety and depression overlapping with those found in posttraumatic stress disorder [PTSD; 6]. There exists very little research on the individual treatment of adjustment disorders in general [7], and none stemming specifically from romantic partner betrayal, despite it being a *universal* injury representing one of the most common reason for seeking psychological help. To address this research gap, we present the rationale, methodological approach, and implications of a novel treatment protocol inspired by the treatment of patients suffering from PTSD that draws upon reconsolidation theory.

Adjustment disorder is classified among the trauma- and stressor-related disorders in the fifth edition of the *Diagnostic and Statistical Manual for Mental Disorders* (*DSM-5;* APA, 2013), and is defined as a maladaptive emotional and behavioral response to a critical change in life's circumstances, such as such as job loss or divorce. Adjustment disorder is the *common cold*

of psychiatry, with prevalence estimates ranging from 5-20% among outpatient mental health services users [8] and 0.9-1.4% in community samples [9]. Left untreated, the disorder is associated with decreased quality of life as well as increased risk for suicide and other mental health disorders [6, 9, 10].

The clinical presentation of adjustment disorder includes symptoms asssociated with PTSD, depression, anxiety, and conduct disturbances. Adjustment disorder can also define a population that meets the full symptom profile of PTSD (e.g., re-experiencing/intrusions, avoidance, hypervigilance/arousal, cognitive distortions), but in response to a an event that does *not* meet its life-threat trauma criterion [e.g., Criterion A; 6]. In line with this, research [11-13] reveals that relationally betrayed individuals report clinically significant symptoms on widely used measures of event-related stress, such as the Impact of Event Scale [IES; 14] and its revised version [IES-R; 15]. For example, Roos et al. [12] examined the association between infidelity in the past 5 years and current self-reported psychiatric symptoms in a small sample of undergraduates: 51% scored above the clinical threshold on the IES-R. These elevated scores were also significantly associated with the severity of depression and anxiety symptoms, even after controlling for prior trauma exposure. Symptoms of intrusions, avoidance, and increased vigilance may be particularly problematic for these individuals [3, 11]. Others found that betrayal was significantly and uniquely predictive of major depression and generalized anxiety disorder in the injured partner [16-18]. Such findings support the notion that betrayal events can precipitate an adjustment disorder.

Current treatment for adjustment disorders and romantic partner betrayal

The treatment of adjustment disorder is not well systematized. Because adjustment disorder is defined as time-limited, persisting no more than 6-months once the stressor has terminated [6],

brief psychotherapy, such as cognitive behavioral therapy is often recommended, however evidence for their efficacy is limited [7, 19]. Additionally, such treatment requires an intense personal investment, is costly, and is not always available in primary care settings where most adjustment disorders are diagnosed [10, 20]. Furthermore, the psychological sequelae of romantic betrayal may, in many cases, be related to additional enduring financial, legal, or social consequences of relationship dissolution, which can not only influence the chronicity of symptoms and functional impairment, but also jeopardize the success of future intimate relationships. Although adjustment disorder is sometimes treated with antidepressants and/or anxiolytics, such treatments essentially mask the symptoms of the disorder without targeting its underlying mechanisms; they must therefore be taken on a daily basis for a considerable amount of time, with ensuing side-effects and compliance problems [21].

Empirical treatments for the effects of betrayal have largely focused on the evaluation of dyadic interventions based on the restoration of interpersonal safety and trust [3, 22]. Although results from such studies have shown promise [3, 11, 23], these interventions were primarily designed for treatment-seeking couples. Many individuals affected by betrayal may not, however, wish to stay in the relationship and would rather seek individual help. Taken together, these limitations highlight the need for individualized therapeutic approaches that are briefer, less costly, and more tolerable. One avenue that has yet to be investigated is reconsolidation therapy, a procedure that has been used with success in the treatment of phobias [24], drug craving [25], and PTSD [26].

Adjustment disorders as the expression of a pathogenic memory

Adjustment disorders can be conceptualized from the standpoint of learning and memory since, like PTSD, they require the experience of an identifiable stressor as part of their etiology [6].

This life experience is stored in the form of a negatively valenced emotional memory that elicits event-related dysphoric symptoms of intrusion, avoidance, hyperarousal, and alterations in cognition and mood [27, 28]. The emotional memory itself is an etiological factor from which stem the symptoms considering that, presumably, if the memory did not exist, neither would the symptoms. Therefore, decreasing the strength of the memory appears to be a desirable outcome likely to reduce the expression of symptoms.

Reconsolidation theory suggests that when a consolidated memory is recalled, under certain circumstances it becomes labile again, and must be reconsolidated in order to persist [29, 30]. As shown in a recent review and meta-analysis, interfering with the reconsolidation process, with the reconsolidation blocker propranolol for instance, will yield a degraded memory trace in animals, healthy humans, and patient populations [31, 32]. This has been recently demonstrated in a double-blind randomized controlled trial, which showed that six weekly 10-25minute sessions of trauma-memory reactivation under propranolol significantly reduced PTSD symptoms below clinical levels when compared to similar trauma reactivation under placebo [26]. Considering that romantic partner betrayal can precipitate event-related stress symptoms stemming from a pathogenic memory, it stands to reason that reconsolidation therapy could be useful to treat this disorder. No research has investigated this question to date.

Study objectives and hypotheses

We aim to investigate the effectiveness of reconsolidation therapy using propranolol to treat adjustment disorders stemming from romantic partner betrayal. As the primary hypothesis, we predict a significant effect of pre-reactivation propranolol treatment compared to a waitlist group in reducing event-related stress symptoms, in an intention-to-treat analysis. Secondary outcomes

will include the impact of treatment on self-rated anxiety and depressive symptoms and quality of life.

Methods / Design

The trial consists of a single-group cross-over design and includes a screening session, a 4-week waitlist, a 4 to 6-week treatment phase, a post-treatment assessment, and a 3-month follow-up (see Additional File 1 for the SPIRIT Checklist, Appendix A). After providing verbal informed consent, candidate participants will be screened over the phone via a brief standardized interview procedure. Apparently eligible individuals will be invited for a face-to-face eligibility assessment conducted by trained doctoral candidates. During this assessment, written informed consent will be obtained, and participants will undergo a structured clinical interview to establish their adjustment disorder diagnosis, evaluate psychiatric comorbidity, and determine if any exclusion diagnoses are met. Participants will then complete a battery of self-report symptom measures prior to being medically evaluated by the study physician to ensure they can safely receive propranolol. All assessments will take place at the Douglas Mental Health University Institute.

Randomization, blinding, and allocation

A typical waitlist design involves randomly allocating study participants in *parallel*, where one group receives the intervention immediately, while a second group waits a pre-determined amount of time before receiving the intervention [33]. One drawback of this study design is that participants are not treated exactly the same way, thereby introducing unknown biases, such as differential expectancy effects [34]. To treat all participants similarly, one approach consists of systematically placing *all* participants on the waitlist before receiving the experimental treatment, and monitor treatment expectancy. This not only addresses several inherent biases in

waitlist-controlled trials, but also allows to determine the stability of baseline level of symptom severity and provide a control condition.

Randomization to 'waitlist group' or 'treatment group' will be done by a blinded third-party uninvolved in participant enrollment or assessment in a post-hoc manner at the time of the statistical analyses. The outcome assessor will also be blind to allocation for the duration of the trial. The randomization scheme will use the permuted-block method with a block size of four, stratified by gender (male and female) and event type (infidelity and other), and a group allocation probability of 50% [35], which will be computer-generated using a random number schedule. A sensitivity analysis will be conducted via a cross-over method, whereby the group allocation will be reversed, and all outcome data will be re-analyzed.

Participants and setting

Participants will be 18-65 years old treatment-seekers with a *DSM-5* [6] adjustment disorder diagnosis stemming from a non-life-threatening betrayal event that occurred within the context of a longstanding (≥ 6 months) exclusive romantic relationship. Betrayal is operationalized as an event where one partner violated the assumption of trust and safety in the romantic relationship, i.e., infidelity or sudden physical abandonment. French- and English-speaking candidates will be recruited via flyers and advertisements, as well as online and through media outlets.

Eligible participants will report clinically significant event-related stress symptoms, as defined by a score > 24 on the IES-R [36], and functional impairment, as defined by a score of at least 'moderately ill' on the Clinical Global Impressions – Severity scale [CGI-S; 37]. Exclusion criteria, drawn from Brunet et al. [26], include: basal systolic blood pressure < 100mmg, basal cardiac rhythm < 55 beats per minute, women who are pregnant or breast-feeding, use of a psychotropic medication (e.g., antidepressants), presence of a medical condition or use of a

medication contraindicated with propranolol, past or present bipolar disorder, psychotic disorder, substance dependence disorder, or active self-harm/suicidality. Participants will be free to continue or pursue other forms of psychotherapy during the waitlist phase of the study but will be required to suspend such participation during the experimental treatment phase.

Intervention: Reconsolidation Therapy treatment protocol

As per the treatment manual (Brunet and Lonergan, unpublished manuscript), on their first treatment session, participants will receive oral propranolol under medical supervision and complete several self-report questionnaires. Sixty minutes later, they will write a 1-page summary of the betrayal event focusing on the hot spot, in the first person, present tense, which will be read aloud to the investigator with the purpose of reactivating the memory under novel conditions promoting mismatch [38], and according to a procedure described elsewhere [39]. Provided that participants tolerate the drug well on their first session, they will subsequently self-administer the propranolol at home 1 hour before the treatment sessions. By tolerating the drug well, we mean that they do not experience any significant side effects that would jeopardize their safety according to the study doctor. Considering that the treatment of adjustment disorder might require fewer treatment sessions than PTSD, a minimum of 4 sessions will be provided. A 5^{th} or 6^{th} treatment session will be offered upon request, if residual symptoms persist. Participants will be offered a list of mental health resources upon the trial's completion should they wish to receive further care.

To ensure protocol adherence, participants will be reminded by phone or text message when the time comes to take their propranolol. Upon arrival to their treatment session, participants' symptoms will be evaluated via self-report questionnaires. Next, they will edit (i.e., add any new details that has bothered them during the week) and read their script out loud to the

interviewer once. Importantly, the interviewer will not attempt to interpret or re-structure the event for the participant, as in standard psychotherapy. The goal of the editing and reading exercise being to effectively reactivate the memory under novel conditions promoting mismatch. At the end of the treatment session, which typically lasts 10-25 minutes, participants will be congratulated on having accomplished a challenging task and be informed that the session is over; that they can unwind in the waiting room and leave whenever they feel ready.

Drug dosage, timing, and side effects

Propranolol is an anti-hypertensive beta-adrenergic receptor blocker that reduces sympathetic activity. It crosses the blood-brain barrier, exerting central as well as peripheral effects. Drug dosage for this study is set at 1 mg/kg based on prior research [26], for non-obese individuals. For obese individuals the dosage will be capped, considering that propranolol is not metabolized by fat tissue [40]. An oral dose of 40-80 mg produces a peak blood level of approximately 100 ng/ml after 75 minutes [41], such that propranolol reaches peak blood plasma concentrations when the memory is reactivated at the time of the script reading, a point at which the memory trace should be maximally labile and its reconsolidation impaired. Propranolol will be ingested with a light snack to enhance bioavailability [42]. Side effects and adverse reactions, if any, will be treated on a case by case basis, documented in the participant's file, and reported to the appropriate regulatory committees.

Assessment measures and outcomes

Table 1 displays the assessment measures administered at each study visit. All measures were chosen for their sound psychometric properties in English and French.

Table 1. Scheduling of assessments and procedures.

	Enrollment		Intervention			Follow-up	
Visit	0	Waitlist	1	2 to 4	5 & 6 (Optional)	7	8
Week	1	1-5	5	6 - 8	9 - 10	11	23
ELIGIBILITY							
MINI-S; SBQ-R; CGI-S	X						
Medical evaluation	X						
ASSESSMENTS							
CEQ		X					
IES-R	X	X	X	X	X	X	X
HSCL-25	X	X	X	X	X	X	X
WHOQOL-Bref	X		X			X	X
INTERVENTION							
Propranolol administration			X	X	X		
Script writing			X				
Script reading			X	X	X		

MINI-S = Mini International Neuropsychiatric Interview-Simplified; WHOQOL-Bref = World Health Organization: Quality of Life, Bref; IES-R = Impact of Event Scale-Revised; HSCL-25 = Hopkins Symptom Checklist-25; SBQ-R = Suicide Behaviors Questionnaire-Revised; CGI-S = Clinician Global Impressions – Severity scale; CEQ = Credibility / Expectancy questionnaire.

Eligibility assessment: Psychiatric comorbidity

The Mini International Neuropsychiatric Interview-Simplified [MINI-S; 43] for *DSM-5* will be used to confirm diagnosis at intake and examine lifetime 'axis I' comorbidity for study eligibility; the following conditions will be assessed: major depressive disorder, adjustment disorder, panic disorder, PTSD, generalized anxiety disorder, social anxiety disorder, alcohol or

drug dependence disorder. The CGI-S is a widely used clinician-rated measure of severity of illness that will be used to confirm level of functional impairment. The Suicide Behaviors Questionnaire-Revised [SBQ-R; 44] will be used to screen for suicidality. Participants at imminent risk for suicide will not be included in the study. Individuals with a detailed plan, an intention to implement the plan, and the means to carry it out, will be immediately brought to the psychiatric emergency of the study premises to receive acute care.

Primary outcome measure

The primary clinical outcome measure will be the widely used IES-R [15], which assesses subjective distress in response to a stressful or traumatic event. The IES-R contains 22 self-report items capturing three symptom clusters of PTSD: Intrusion, Avoidance, and Hyperarousal. Items are rated for the past week using a 5-point scale (0 = Not at All to 4 = Extremely). Total severity scores (range: 0-88) are obtained by summing all items. The IES-R has been used before to assess the impact of events such as betrayal [12, 13] and romantic separation [45].

Secondary outcome measures

Symptoms of anxiety and depression, as well as perceived quality of life, will be assessed. For anxiety and depression, the self-report Hopkins Symptom Checklist-25 [HSCL-25; 46] will be used with respect to the past week. For quality of life we will use the self-report World Health Organization's measure [WHOQOL-Bref; 47] assessing perceived quality of life in four domains (physical, psychological, social, environment) for the past 2 weeks.

Treatment expectancy

As recommended [see 33], we will monitor treatment expectancy in order to examine possible threats to internal validity using the 6-item Credibility / Expectancy self-report questionnaire [CEQ; 48].

Data handling, record keeping, participant compensation, and criteria for discontinuation

To protect confidentiality, a numerical code will be assigned to each study participant. The list matching the names and numerical codes will be kept separate from the questionnaires. Completed questionnaires will be stored in a locked file cabinet or password protected computers. Access to the lists of names and to the questionnaires will be restricted to research personnel who are working on the present study. Confidentiality might be broken in the event that the information provided to the investigator involves planned harm to oneself or others. The law requires that such information be reported to legal authorities. Any changes to the protocol will be subjected to review and require approval from the Douglas research ethics board and Health Canada prior to implementation. With over 15 years of experience in conducting similar clinical trials in patient populations with PTSD, the primary investigator and trial physician will be responsible for data and participant monitoring.

Participants will be compensated for their participation. Any communication from the participant, whether received verbally or in writing in which the participant states that he/she wishes to withdraw from the study will lead to the cessation of all study procedures. Reasons for withdrawal, if provided, will be documented in the case report form. Participants may be withdrawn at any time from the study. Reasons of discontinuation include the following:

1. The participant is repetitively non-compliant with the protocol.
2. The participant develops a concurrent illness, which, in the opinion of the investigator, warrants discontinuation.
3. The participant enrolls into another drug trial during the course of the study.
4. In the opinion of the investigator, the participant's symptoms significantly deteriorate. In such cases participants will be referred to other forms of care.

Statistical power and analyses

We will rely on an intention-to-treat (ITT) analysis for the main analyses, which retains the intended effect of randomization and creates study arms that are not systematically different on known and unknown prognostic factors, thus providing an unbiased estimation of intervention effects. All randomized participants will be included in the ITT sample. Patterns of missing data will be inspected, and multiple imputations will be performed provided that the data is missing completely at random.

Analysis of covariance (ANCOVA) will be used to test the between group mean difference on post-waiting list/treatment IES-R scores, controlling for baseline IES-R scores. Assuming a Type I error rate of .05 in a two-sided test for the group main effect of an ANCOVA model, with a sample of 60 individuals, we will have .85 power to detect an effect size of $f = .40$. This represents a clinically meaningful change, as measured by a mean pre-post difference score of 15 points on a self-report symptom measure like the IES-R, or 1 standard deviation, as has been obtained by others [26, 49]. Secondary outcomes, the HSCL-25 and WHOQOL-Bref will be explored and analyzed in a similar way as the primary outcome. All ITT analyses will be repeated using a per protocol (PP) approach. This will include all participants who completed at least 4 treatment sessions, whose treatment did not significantly deviate from the manualized treatment protocol, and who did not meet an exclusion criterion during the course of the study. In a sensitivity analysis, we will reverse group allocation and re-analyze all outcome data in both the ITT and PP approach. We will also examine and control for the influence of treatment expectancy, duration of relationship, and time since the event on outcome.

Discussion

Romantic betrayal is a devastating life-event that can precipitate significant event-related stress symptoms, including depression, anxiety, PTSD-like symptoms, and functional

impairment [12, 13, 16-18]. Extending the use of reconsolidation therapy to this form of adjustment disorder fills an important gap in developing and testing a therapeutic protocol for which no validated specific treatment currently exists. Reconsolidation therapy is a brief, inexpensive intervention that is safe, easy to administer, and has demonstrated efficacy in several clinical trials investigating its application to a range of psychiatric disorders that are rooted in powerfully conditioned emotional memories [26, 50]. The design of this trial will permit the investigation of the effectiveness of reconsolidation therapy is a more naturalistic clinical setting and provide the foundation for larger placebo-controlled trials. If this treatment proves effective for adjustment disorders, it can be implemented by mental health professionals from a variety of clinical backgrounds and has the potential to reach a wide population of trauma or stressor-exposed individuals. Importantly, reconsolidation therapy can be used as a stand-alone treatment or in conjunction with currently available individual and couple's psychotherapies, potentially increasing their effectiveness.

The current study also carries important theoretical implications. Adjustment disorder recently moved under the trauma- and stressor-related disorders category in the *DSM-5*, highlighting the recognition that a range of life stressors can precipitate posttraumatic pathology. However, the construct of adjustment disorder remains under-researched, leading to difficulties in determining appropriate and effective treatment avenues [10]. Importantly, this study will provide insights into the conceptualization of adjustment disorders as the clinical expression of a pathogenic memory, as well as the role of betrayal in perpetuating adjustment disorders. Findings from this study may re-ignite interest in further understanding the epidemiology, diagnosis, and treatment of distress stemming from negative life-events.

Trial Status:

This protocol received a No Objection Letter from Health Canada on May 15th, 2015 and was approved by the Douglas Mental Health University Insitute research ethics board on May 20th 2015. Recruitment began in November 2015, and is still active.

Abbreviations:

PTSD: Posttraumatic stress disorder

DSM-5: Diagnostic and Statistical Manual for Mental Disorders, 5th Edition.

IES-R: Impact of Event Scale-Revised

IES: Impact of Event Scale

CGI-S: Clinical Global Impressions – Severity scale

MINI-S: Mini International Neuropsychiatric Interview-Simplified

SBQ-R: Suicide Behaviors Questionnaire-Revised

WHOQOL-Bref: World Health Organization Quality of Life-Bref scale

CEQ: Credibility / Expectancy Questionnaire

ITT: Intention-to-treat analysis

PP: Per Protocol analysis

ANCOVA: Analysis of Covariance

Declarations:

Ethics approval and consent to participate:

The study received approval from the Douglas Mental Health University Institute research ethics board (REB# 15-07) and a No Objection Letter from Health Canada (control# 183228).

Consent for publication:

Not applicable.

Availability of data and materials:

The datasets used and / or analysed during the current study will be available from the corresponding author on reasonable request.

Competing interests:

The authors report no financial or non-financial conflicts of interest.

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Author contributions:

M.L and A.B. conceptualized the design, are coordinating and implementing the study, and drafted the manuscript. E.M. participated in drafting the manuscript. D.S. assisted in the conceptualization and implementation of the study design, assisted in its implementation, and helped draft the manuscript. S.P. is participating in data collection, monitoring, implementing the protocol, and preparing the manuscript for publication. N.J. participated in editing and reviewing the manuscript.

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Transitional text #1

The previous manuscript presented the study protocol for investigating the effectiveness of reconsolidation therapy using propranolol to treat adjustment disorders stemming from romantic partner betrayal via a waitlist-controlled clinical trial. Providing scientific transparency and the ground work for future replication studies, this paper not only disseminated the reconsolidation therapy treatment procedure, but also described a novel method for employing waitlist-controlled designs. Usually, in waitlist-controlled trials, participants are not treated in the same manner from the outset; they are randomized at study entry to either receive the active treatment immediately, or to wait a pre-determined amount of time before receiving the treatment. However, research reveals that telling treatment-seeking participants to 'wait' to change may stall their progression; waitlist control participants have been found to improve less than what would be expected under natural conditions (Cunningham, Kypri, & McCambridge, 2013). A recent meta-analysis of cognitive behavioral therapy for depression (Furukawa et al., 2014) revealed that comparison participants in 'no treatment' controlled trials (i.e., trials in which control participants were told they would not receive the experimental treatment) demonstrated more improvement compared to those in waitlist-controlled trials (i.e., trials where participants were told they would receive the experimental treatment at the end of a waitlist period). It is suggested that the differential treatment of participants may influence outcome expectancies between the delayed and immediate treatment groups, thereby upwardly biasing treatment effects (Cunningham et al., 2013; Mohr et al., 2009).

In Chapter 3, a novel method of employing a waitlist-control condition was proposed that involves 1) systematically placing all participants on the waiting list, thus treating them in exactly the same manner, 2) advising participants that they are free to engage in or continue with other forms of therapeutic intervention while on the waiting list, and 3) monitoring and

statistically controlling for treatment expectancy. Randomization is conducted by a third party, unrelated to the study and blinded to participant outcome, and sensitivity analyses involve reversing the random group allocation and re-analysing treatment data in a cross-over approach. The randomization scheme employs a permuted block method with a pre-determined block-size (Fleiss, 1986), counterbalanced across certain sociodemographic factors (e.g. gender, event type), and temporal order of participant enrollment is maintained to control for the effects of change over time (Handley, Lyles, McCulloch, & Cattamanchi, 2018). This method utilizes outcome data from all participants, thereby increasing statistical power. Additionally, it is likely that individuals receiving this treatment in clinical practices may be required to wait several weeks before starting treatment, thus this method also increases ecological validity. The next manuscript presents the results of this investigation.

Chapter 4

Eternal Sunshine of the Spotless Mind: A waitlist-controlled clinical trial of reconsolidation therapy to treat adjustment disorder following romantic betrayal.

"The brain is a far more open system than we ever imagined, and nature has gone very far to help us perceive and take in the world around us. It has given us a brain that survives in a changing world by changing itself."

– Normand Doidge, The Brain that Changes Itself

Lonergan, M., Saumier, D., Tremblay, J., Pigeon, S., Etienne, P., & Brunet, A. Eternal Sunshine of the Spotless Mind: A waitlist-controlled clinical trial involving reconsolidation therapy to treat adjustment disorder following romantic betrayal. [Manuscript in preparation for *Journal of Consulting and Clinical Psychology*].

Abstract

Objective: While romantic partner betrayal can lead to an adjustment disorder in some individuals, few treatments exist. Disrupting memory reconsolidation with the noradrenergic beta-blocker propranolol has been shown to dampen the enhancing effects of emotion on memory and alleviate event-related stress symptoms in patient populations with posttraumatic stress disorder. Here, we investigated the effectiveness of reconsolidation therapy using propranolol to treat adjustment disorder stemming from romantic partner betrayal.

Method: In a waitlist-controlled randomized clinical trial, we hypothesized that the treatment group would improve significantly more than the waitlist group on measures of event-related stress symptoms and psychological distress. Participants received 4 to 6 weekly sessions of betrayal-memory reactivation under propranolol. Clinical outcomes included the Impact of Event Scale Revised to measure event-related stress, the Hopkins Symptom Checklist-25 to measure depression and anxiety, and the World Health Organization Quality of Life-Bref to measure satisfaction with quality of life and well-being.

Results: Compared to participants in the waitlist-condition (n = 29), reconsolidation therapy under propranolol (n = 30) produced a statistically significant and clinically meaningful decrease in event-related stress symptoms, as well as general psychological distress. The treatment also led to improvements in selected domains of quality of life.

Conclusion: Results support the clinical usefulness of reconsolidation therapy to treat event-related stress symptoms that may result from relational betrayal. Larger placebo-controlled clinical trials would be warranted to further establish the treatment effect. Our findings extend the usefulness of reconsolidation therapy beyond traumatic stress.

Keywords: Romantic betrayal, adjustment disorder, reconsolidation, propranolol, clinical trial.

Public health significance:

This research suggests that romantic partner betrayal may precipitate an adjustment disorder in the injured party, characterized by event-related stress symptoms (intrusions, avoidance, increased vigilance), depression, anxiety, and functional impairment. Compared to a waitlist control condition, reconsolidation therapy using propranolol significantly attenuated adjustment disorder symptoms among relationally betrayed individuals. Results from this study support the continued investigation of this treatment for stressor-related psychiatric symptoms rooted in the experience of negative and distressing life events.

Introduction

Intrusive thoughts, images, and memories of distressing life experiences can underlie a range of psychopathology (Brewin, Gregory, Lipton, & Burgess, 2010; Marks, Franklin, & Zoellner, 2018). One particularly devastating life-event, romantic partner betrayal (e.g., infidelity, sudden abandonment), is a common occurrence with far reaching negative implications for mental health. Experts argue that similar to psychological trauma, betrayal shatters fundamental assumptions of safety and trust in the self and others, and as such, can be especially difficult to overcome (Gordon, Khaddouma, Baucom, & Snyder, 2015; Johnson, Makinen, & Millikin, 2001). Indeed, some injured individuals often report enduring symptoms of intrusions/re-experiencing, avoidance, increased vigilance and arousal, negative cognitions, as well as anxiety and depression in the aftermath of betrayal (Cano & O'Leary, 2000; Kroger, Reisner, Vasterling, Schutz, & Kliem, 2012; Laaser, Putney, Bundick, Delmonico, & Griffin, 2017; Roos, Willetts, Canavello, & Bennett, 2017; Steffens & Rennie, 2006; Whisman, 2015). Such a syndrome falls into the new trauma-and stressor-related disorders category of the 5th edition of the *Diagnostic and Statistical Manual for Mental Disorders* as an adjustment disorder (*DSM-5*; American Psychiatric Association [APA], 2013). Similar to posttraumatic stress disorder (PTSD), adjustment disorder is characterized by stress-related emotional and behavioral symptoms, however in contrast to PTSD, the stressor does not involve life-threat (APA, 2013; Maercker & Lorenz, 2018). The prevalence of adjustment disorder ranges from 5% - 20% in primary care settings, and it is often considered the ‘common cold’ of psychiatry; despite this, empirically validated specialized treatments are scarce (APA, 2013; O'Donnell, Metcalf, Watson, Phelps, & Varker, 2018; Zelviene & Kazlauskas, 2018).

Although several research teams have been developing betrayal-specific dyadic interventions (Gordon, Baucom, & Snyder, 2004; Halchuk, Makinen, & Johnson, 2010; Makinen & Johnson, 2006), these approaches do not directly target the core stressor-related symptoms, such as intrusive thoughts, images, and memories, which may be particularly problematic in this population (Kroger et al., 2012; Roos et al., 2017; Steffens & Rennie, 2006). Further, considering that separation or divorce is 2 to 4 times more likely to occur when betrayal is involved, many individuals may not wish to enter couple's therapy (Adamopoulou, 2013; Allen & Atkins, 2012). While experts argue that the steps and procedures involved in dyadic interventions can be translated to individual psychotherapy, research supporting this assertion is scarce. To our knowledge, there exists no individualized intervention to treat the adverse effects of romantic betrayal.

One intervention that has yet to be investigated stems from pathogenic memory models of event-related distress (Maercker & Lorenz, 2018; Marks et al., 2018). Emotional events are better remembered, in part, due to increased activation of endogenous stress hormones (e.g., noradrenaline) within the amygdala during initial learning, which potentiates memory consolidation (i.e., the stabilization of memory into long-term storage) and facilitates later recall (McGaugh, 2004, 2013). Initially thought to be stable and permanent, it is now well-established that under certain conditions, memories return to a labile state upon retrieval and must reconsolidate to persist; as in initial consolidation, the reconsolidation of emotional memories involves the reactivation of the noradrenergic system within the amygdala and subsequent *de novo* protein synthesis (Lee, Nader, & Schiller, 2017; Lim et al., 2018; Nader, Schafe, & Le Doux, 2000). Dysregulation of these emotional memory mechanisms may lead to persistent hypermnesia of a highly distressing event, which perpetuates clinically significant event-related

stress symptoms of intrusive re-experiencing, avoidance, and increased vigilance (Brewin et al., 2010; Iyadurai et al., 2018; Marks et al., 2018). Considering that the neural circuits involved in emotional memory maintenance are also activated when one experiences personal deception (Grezes, Berthoz, & Passingham, 2006), or is presented with reminders of unrequited love (Fisher, Brown, Aron, Strong, & Mashek, 2010), it is possible that the memory of the betrayal or abandonment event underlies, in part, the resulting pathology.

Reconsolidation theory offers new hope for the treatment of psychiatric symptoms rooted in emotional or distressing memories. When administered in conjunction with memory retrieval, propranolol, a noradrenergic beta-blocker, dampens the enhancement of memory conferred by emotion, presumably by disrupting its reconsolidation (Lonergan, Brunet, Olivera-Figueroa, & Pitman, 2013). Translated to clinical populations, Brunet et al (2018) recently demonstrated that six 10-25minute weekly trauma-memory reactivation sessions under propranolol (henceforth called, reconsolidation therapy) significantly alleviated posttraumatic stress disorder (PTSD) symptoms compared to the same protocol experienced under placebo. Further evidence of its therapeutic potential comes studies of specific phobia (Soeter & Kindt, 2015) and substance dependence (Lonergan et al., 2016). In the present study, we investigated whether reconsolidation therapy using propranolol can alleviate adjustment disorder symptoms among relationally betrayed men and women. We predicted that compared to a no-treatment waitlist control, reconsolidation therapy would significantly reduce event-related stress symptoms and general psychological distress. We also explored the effects of treatment on quality of life.

Method

This waitlist vs. treatment randomized trial (clinicaltrials.gov NCT03151681) was approved by the Douglas Institute Research Ethics Board and by Health Canada. Full details of

the study protocol are provided in Lonergan et al. (submitted). In short, consented treatment-seeking adults (18-65 years) meeting *DSM-5* adjustment disorder criteria of the Mini International Neuropsychiatric Interview-Similified (MINI-S; Lecrubier et al., 1997) were recruited following an abrupt betrayal event (i.e., infidelity, sudden physical abandonment) that occurred in the context of a committed romantic relationship lasting at least 6 months in duration. The exclusion criteria were: basal systolic blood pressure < 100mmg, basal cardiac rhythm < 55bpm, pregnancy/breast-feeding, psychotropic medication use, a medical counter-indication, and significant psychiatric comorbidity (e.g., major depressive disorder or PTSD), or active self-harm/suicidality. The randomization scheme, created by a third-party blinded to participant outcome, was stratified by gender and event type, used the permuted-block method with a block size of four and a 50% group allocation probability (Fleiss, 1986).

The trial consisted of an initial eligibility assessment, a 4 to 5-week waitlist period (M = 4.43, SD = .98), and 4 to 6 weekly sessions of reconsolidation therapy under propranolol. The post-treatment assessment was conducted 1-week after the last treatment visit and a follow-up occurred after 4 months. During the first treatment session, participants received 1mg / kg of short-acting propranolol at the Douglas Institute, administered by the nurse. Their vital signs (blood pressure and heart rate) were monitored immediately prior to drug intake and every 30 minutes for 60 minutes. After 60 minutes, participants wrote a one-page summary of the betrayal event in the first person present tense, focusing on describing the hot spot, which they subsequently read aloud once to the investigator. In the subsequent sessions, if they were comfortable doing so, participants took the study drug at home 60 minutes prior to their scheduled appointment. They were reminded to take their medication via phone call or text message. Upon arrival to their appointment, participants completed the self-report symptom

measures and then read their narrative out loud to the interviewer. Once the reading exercise was complete, participants were congratulated on accomplishing a difficult task, and were asked how they felt and whether they wished to modify their narrative (see treatment manual of Brunet & Lonergan, unpublished). All sessions were conducted at the Douglas Institute.

In line with prior work in similar populations (e.g., Kroger et al., 2012; Roos et al., 2017), we opted for the self-report Impact of Event Scale – Revised (IES-R; Weiss & Marmar, 1997) as the primary clinical outcome to assess severity of event-related stress symptoms over the past 7 days in response to a specific stressor. A total severity is score is obtained by summing item scores (range: 0 – 88), and 33 is the widely used cut-off to indicate possible PTSD (Creamer, Bell, & Failla, 2003). Secondary self-report outcomes included the Hopkins Symptom Checklist-25 (HSCL-25; Winokur, Winokur, Rickels, & Cox, 1984) to measure general psychological distress, and the World Health Organization's Quality of Life-Bref measure (WHOQoL- Bref; Skevington, Lofty, & Connel, 2004). The HSCL-25 measures symptoms of depression and anxiety, while the WHOQoL-Bref assesses satisfaction and well-being in four domains of quality of life: Physical (e.g., mobility, pain and discomfort, energy and fatigue, work capacity, dependence on medical substances or medical aid, activities of daily living, sleep and rest), Psychological (e.g., body image, negative / positive feelings, self-esteem, spirituality, concentration), Social (e.g., personal relationships, social support, sexual activity), and Environmental (e.g., financial resources, physical safety, health and social care, home environment, opportunities of acquiring new skills, participation in leisure activities, physical environment, transport). The Credibility / Expectancy questionnaire (CEQ; Devilly & Borkovec, 2000) was used to monitor treatment expectancy.

Statistical Analyses

To retain the effect of randomization and produce unbiased estimates of treatment effects, we employed an *intent-to-treat* (ITT) analysis (see Gupta, 2011), which consisted of all randomized participants ($N = 59$). Multiple imputations were used to account for missing data on the post-treatment IES-R and HSCL-25. Approximately 16% of values were missing, therefore 20 imputed data sets were created to minimize over-estimation of the standard errors and reduce bias (Graham, Olchowski, & Gilreath, 2007). All baseline demographic and clinical variables were included in the imputation model as predictor variables; CEQ-Expectancy scores and all longitudinal data from the IES-R and HSCL-25 were both imputed and used as predictors. Missing data was at least missing at random (Little's MCAR test, $\chi^2 = 150.56$, $df = 156$, $p = 0.608$). There were no significant differences between participants who dropped out of the treatment and treatment completers on any variable. The Fully Conditional Specification (FCS) method, which employs an iterative Markov Chain Monte Carlo algorithm using predictor and imputed values at one step to impute missing values in subsequent steps, was used. Constraints were placed to ensure that the imputed values did not exceed the measures' range. The relative efficiency of the imputation models ranged between 98% and 99%, and inspection of the FCS iteration graphs indicated that model convergence was achieved.

A series of one-way analysis of covariance (ANCOVAs) were conducted on post-treatment total IES-R scores and total HSCL-25 scores, controlling for baseline symptom severity. The presumed time-constrained course of adjustment disorder (e.g., 6 months; APA, 2013), as well as the duration of the romantic relationship, may influence the severity of participants' symptoms and treatment outcome, and treatment expectancy is proposed to be a critical component of treatment response (Price et al., 2015). Therefore, we also examined and

statistically controlled for possible confounding effects of time since the event, duration of the relationship, and treatment expectancy on outcome. All analyses were repeated in a *per protocol* (PP) sample, which included all participants who completed at least 4 treatment sessions and whose participation and treatment did not significantly deviate from the research and treatment protocols ($N = 29$). A sensitivity analysis was conducted by reversing group allocation in a modified cross-over method and re-analyzing all outcome data in the exact same manner as the primary analysis. Alphas were set at .05 (two-tailed), and Bonferroni corrections were applied when necessary. Analyses were conducted using SPSS v. 25. Pooling procedures outlined in van Ginkel and Kroonenberg (2014) were followed to obtain pooled *F*-values, parameter estimates, and degrees of freedom, with the SPSS Macro obtained from https://www.universiteitleiden.nl/en/staffmembers/joost-van-ginkel#tab-1.

Results

Table 1 displays the sociodemographic and baseline clinical data of the sample by group. Figure 1 depicts the participant flow chart (see also Appendix B). This sample was recruited from 05/2015 until 10/2017; 59 participants were randomized and received an average of 4.67 ($SD = 2.45$) treatment sessions; 44 participants completed 4 treatments, 43 completed 5 treatments, and 41 completed 6 treatments. In the PP sample, all participants received 6 treatments, except for 1 who received 5 treatments. Baseline sociodemographic and clinical variables were compared between groups using independent *t*-tests (or equivalent Mann-Whitney *U* tests) for continuous variables, and Fisher's exact or chi-square tests for categorical variables. All outcome data approximated a normal distribution, and there were no outliers.

Effects of Treatment on Self-Report Event-Related and General Psychological Distress

There was no evidence of collinearity between the covariates within each level of group (rs ≤ .60, see Appendix C), and no significant between group differences on any covariate. All ANCOVA assumptions were met. Improvement in event-related stress symptoms as measured with the IES-R is presented in Figure 2. Table 2 presents the means and standard errors of the IES-R, and results from the ANCOVA analyses on post-treatment IES-R and HSCL-25 scores, controlling for baseline, are presented in Table 3. Examining the IES-R, there was a significant between-group difference on post-treatment scores ($p < .001$; $d = 1.58$). The pre-post effect size for the waitlist condition was $d = .04$, while the pre-post effect size for the treatment condition was $d = 1.35$ (Figure 2. panels a. and b.). The significant between-group difference on post-treatment IES-R scores remained in the PP sample ($p < .001$; $d = 2.01$); the pre-post effect size for the waitlist condition was $d = .17$, and $d = 2.13$ for the treatment condition.

Results also revealed a significant between-group difference on post-treatment HSCL-25 scores ($p < .001$; Waitlist: $M = 2.20$, $SE = .13$, Treatment $M = 1.65$, $SE = .12$, $d = .81$). The pre-post effect size for the waitlist condition as $d = .13$, and the pre-post effect size for the treatment condition was $d = 1.02$. Similar results were obtained in the PP sample ($p < .001$; Waitlist: $M = 1.99$, $SE = .13$, Treatment $M = 1.40$, $SE = .12$, $d = 1.22$). The within group effect size for the waitlist condition was $d = .04$, and for the treatment condition was $d = 1.49$. Adding duration of relationship, time since the event, and treatment expectancy as covariates to the models did not impact any of these outcomes (see Table 3). Results from the sensitivity analyses did not diverge from these findings (presented in Figure 2 panels c. and d. and in Tables 2 and 3, see also Appendices D and E).

Exploring the IES-R and HSCL-25 Subscales, and WHOQoL-Bref Domains

Given that all participants were placed on the waiting list prior to receiving treatment, *ad hoc* exploratory analyses were conducted on: the 1) IES-R subscale scores (Intrusion, Avoidance, and Hyperarousal), 2) HSCL-25 subscale scores (Depression and Anxiety); and 3) WHOQOL-Bref domain scores (Physical, Psychological, Social, Environmental), to examine within-group change from baseline- to post-waitlist, and post-waitlist to post-treatment among treatment completers (n = 44). A series of repeated measures ANOVAs were conducted, and Greenhouse-Geisser corrections were applied when sphericity was violated. Tables 4. and 5. display the means, standard deviations, and within-group effect sizes for the IES-R and HSCL-25 subscales, as well as the WHOQoL-Bref domains, respectively.

Results from the IES-R subscales revealed a statistically effect of time for the Intrusion subscale ($F_{1.65, 70.99} = 153.09$, $p < .001$, $\eta^2 = .78$), the Avoidance subscale ($F_{1.38, 59.45} = 46.70$, $p < .001$, $\eta^2 = .52$), and the Hypervigilance subscale ($F_{2, 86} = 91.28$, $p < .001$, $\eta^2 = .68$). Results also revealed a statistically significant effect of time for the Depression subscale ($F_{2, 86} = 64.81$, $p < .001$, $\eta^2 = .60$) and the Anxiety subscale ($F_{2, 86} = 32.87$, $p < .001$, $\eta^2 = .43$) of the HSCL-25. Post-hoc pairwise Bonferroni comparisons revealed no significant differences in subscale scores between baseline-and post-waiting list, and significant reductions in all subscale scores between post-waiting list and post-treatment, and between baseline and post-treatment (all ps < .001).

Examining the WHOQoL-BREF, there was a significant effect of time for all domains: 1) Physical ($F_{1.73, 67.58} = 15.15$, $p < .001$, $\eta^2 = .28$); 2) Psychological ($F_{2, 78} = 23.78$, $p < .001$, $\eta^2 = .38$); 3) Social ($F_{2, 76} = 5.11$, $p = .008$, $\eta^2 = .12$); and 4) Environmental ($F_{2, 80} = 4.94$, $p = .009$, $\eta^2 = .11$). Post-hoc Bonferroni adjusted pairwise comparisons were conducted. For the Physical domain, there was no significant difference between baseline and post-waiting list, and a

significant increase in scores between post-waiting list and post-treatment ($p < .001$), and between baseline and post-treatment ($p = .002$). For the Psychological domain, there was no difference between baseline and post-waiting list, and a significant increase in scores between post-waiting list and post-treatment, and between baseline and post-treatment ($ps < .001$). However, for the Social and Environmental domains, while there were significant differences between post-waiting list and post-treatment ($ps < .01$), there were no significant differences between baseline and post-waiting list, or between baseline and post-treatment.

Analysis of Follow-Up Data: IES-R, HSCL-25, and WHOQoL-Bref

Follow-up data was analyzed with a series of Bonferroni corrected paired *t*-tests between post-treatment and follow-up ($n = 32$). Twelve participants were lost to follow-up, with no reason provided. The average time between post-treatment and follow-up was 4 months ($SD = .89$). There were no significant within group differences on total IES-R scores (post-treatment $M = 16.97$, $SD = 11.59$; follow-up $M = 18.46$; $SD = 14.93$, $t_{31} = .80$, $p = .433$), on HSCL-25 scores (post-treatment $M = 1.42$, $SD = .36$; follow-up $M = 1.44$, $SD = .46$; $t_{29} = -.56$, $p = .582$), or on WHOQoL-Bref scores between post-treatment and follow-up (Physical: follow-up $M = 72.53$, $SD = 15.77$, $t_{28} = .39$, $p = .698$; Psychological: follow-up $M = 61.49$ $SD = 17.52$, $t_{28} = -.37$, $p = .711$; Social: follow-up $M = 60.34$, $SD = 21.32$, $t_{28} = .19$, $p = .853$; Environmental: follow-up $M = 72.19$, $SD = 13.86$, $t_{28} = 1.41$, $p = .169$).

Discussion

This study is the first to investigate the effectiveness of reconsolidation therapy using propranolol to treat trauma-and stressor-related disorders beyond PTSD. After being placed on a 4 to 5 week waiting list, individuals meeting criteria for adjustment disorder stemming from romantic partner betrayal received up to 6 weekly sessions of betrayal-memory reactivation 60

minutes after ingesting propranolol. In both the intention-to-treat and per protocol samples, results demonstrated very large and clinically meaningful decreases in event-related stress symptoms, including intrusions, avoidance, and increased vigilance, as well as general psychological distress (e.g., depression and anxiety), when compared to a waitlist control condition. Additionally, treatment effects continued to be significant after controlling for time since the event, duration of relationship, and treatment expectancy, and improvements in selected domains of quality of life were observed (e.g., Physical and Psychological). All treatment gains were maintained at the 4-month follow-up. Overall, the treatment was well tolerated. These findings suggest that reconsolidation therapy using propranolol is a viable treatment option for adjustment disorders that may occur following betrayal by a romantic partner.

Our examination of the effects of reconsolidation therapy on perceived quality of life produced intriguing results that may inspire future research. First, baseline means for the Environmental domain, which evaluates quality of life aspects related to financial resources, physical safety and security, and home environment among others, was comparable to community population norms (Skevington & McCrate, 2012), and remained stable through post-treatment and follow-up. Considering that this sample predominantly consisted of well-educated, middle or upper-income participants with stable employment, this domain of quality of life may have been less affected by betrayal. On the other hand, baseline scores on the Physical, Psychological, and Social domains were much lower than healthy population norms (Skevington & McCrate, 2012), suggesting that certain domains of quality of life may be more affected by betrayal than others. The physical domain evaluates the ability to complete day-to-day tasks, perceived levels of energy, work capacity, and satisfaction with sleep, while the Psychological domain evaluates aspects related to body image, self-esteem, mood, and concentration, and the

Social domain evaluates satisfaction with relationships, social support, and sexual activity (Skevington et al., 2004). Although significant improvements in the Physical and Psychological domains were observed at post-treatment, 17%, 43%, and 29% of participants continued to obtain scores at least 1 standard deviation below healthy population means on the Physical, Psychological, and Social domains, respectively (Skevington & McCrate, 2012). It is possible that more time or additional forms of psychotherapy are warranted in cases where quality of life is more severely disrupted. Indeed, examination of the mean domain scores over time reveals incremental yet steady improvement through the 4-month follow-up, particularly for the Physical domain. Taken together, these findings suggest that reconsolidation therapy may produce improvements in select domains of quality of life, particularly related to physical and psychological well-being, although studies with longer follow-ups are needed.

Findings from this study are consistent with Maercker, Einsle, and Köllner (2007) model of adjustment disorder as a stress-response syndrome characterized by core symptoms of intrusions / preoccupations / avoidance and failure to adapt (see also Maercker & Lorenz, 2018). Most participants not only exceeded the probable diagnostic cut-off of the IES-R at study entry, but also reported total and subscale scores comparable to other trauma exposed populations with PTSD (Rash, Coffey, Baschnagel, Drobes, & Saladin, 2008). Intrusion symptoms appeared particularly problematic in this sample. Notably, they were the most improved. Likewise, subscale scores on the HSCL-25, as well as scores the Psychological and Social domains of quality of life, were similar to clinical populations with diagnosed mood or anxiety disorders (González-Blanch et al., 2018; Mattisson, Bogren, & Horstmann, 2013). Further, participants' symptoms occurred as a direct result of the betrayal event and could not be better explained by another mental health disorder. Moreover, Maercker et al. (2012) revealed that close to 73% of

adjustment disorder cases persisted for at least 2 years, calling into question the presumed time-limited course of the disturbance (e.g., 6 months; APA, 2013). Considering that the average time since the betrayal event was ≈3.5 years, and that this variable was unrelated to baseline symptom severity or outcome, our results also suggest that adjustment disorders may be more persistent than originally thought. These findings further highlight the need for additional research on the course of, and precursors to, adjustment and other stressor-related disorders.

Several limitations of this study should be noted. First, as we did not explicitly examine mechanisms of change, we cannot definitively conclude that the observed treatment gains were entirely due to reconsolidation interference. Further, without a placebo group, we cannot rule out that beneficial treatment effects may have been obtained from repeated retrievals (e.g., exposure) to the event. Although our design is strengthened by its use of a novel method intended to increase the external validity of reconsolidation therapy, the use of waitlist controls in clinical trials may produce upward biases in treatment effect due to the differential treatment of participants at study entry, which may influence outcome expectancies (Cunningham, Kypri, & McCambridge, 2013; Mohr et al., 2009). However, in this study, all participants were treated in the exact same manner and were not dissuaded from receiving other therapeutic interventions while on the waiting list. Moreover, outcome expectancy did not differ between groups, and was unrelated to treatment response. Thus, this threat to internal validity may have been minimized. Thirdly, for the purposes of maintaining the single blind and consistency with prior research in similar populations (Roos et al., 2017), we used the self-report IES-R as a primary measure of traumatic stress symptoms, which may have over- or under-estimated symptom severity. Future investigations via placebo-controlled trials that include more objective clinician-administered measures of adjustment disorder are required to substantiate our findings. Finally, research

suggests not only that the prevalence of stress-related psychopathology is more prevalent among women, but reconsolidation therapy may also be more effective for women (Poundja, Sanche, Tremblay, & Brunet, 2012; Maercker et al., 2012). Future studies employing more diverse samples are needed to examine the generalizability of our findings.

The goal of this study was to examine the effectiveness of reconsolidation therapy in a more naturalistic setting among a sample of individuals suffering in the aftermath of intimate partner betrayal. Romantic relationship distress is a frequent concern faced by mental health professionals, and betrayal events are among the top cited reasons for relationship dysfunction and breakdown (Amato & Previti, 2003; Scott, Rhoades, Stanley, Allen, & Markman, 2013; Snyder & Halford, 2012). In this study, we not only demonstrated that romantic partner betrayal may precipitate an enduring adjustment disorder, but also that reconsolidation therapy using propranolol can reduce event-related stress symptoms, including intrusions, avoidance, and increased vigilance, as well as depression and anxiety, and improve certain domains of quality of life. Reconsolidation therapy is a brief, tolerable, and effective intervention that can be easily learned by a variety of mental health professionals (a treatment manual is available from the primary investigator; see reconsolidationtherapy.com for more information). If incorporated into clinical practice, this intervention has the potential to accelerate recovery for a large population of individuals negatively affected by significant life-stressors.

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Table 1.

Sociodemographic and Clinical Variables by Group

Characteristic	Waitlist (n = 29)		Treatment (n = 30)	
	M	*SD*	*M*	*SD*
Age	39.8	10.9	42.5	12.4
Education (years)	16.9	2.4	17.3	2.8
Time since betrayal event (years)	3.0	3.1	4.1	6.7
Duration of relationship (years)	7.9	9.4	10.8	10.9
	N	*%*	*N*	*%*
Female gender	19	65.5	21	70.0
Ethnicity (% Caucasian)	23	79.3	26	86.7
Annual income (≥ 50k CAD$)	17*	58.6	9*	30
Marital Status (single)	20	69	18	60
Betrayal event				
Infidelity / Deception	21	72.4	22	73.3
Sudden abandonment	8	27.6	8	26.7
Prior / Current use of mental health services	18	62.1	16	53.3
Comorbidity				
Lifetime major depression	11	37.9	12	40.0
Lifetime anxiety disorder	7	24.1	11	37.6
Improvement				
Moderate to none	21	84.0	3	13
Clinically meaningful[a]	4	16.0	20	87
Probable adjustment disorder post-treatment[b]				
Yes	21	84.0	5	21.7
No	4	16.0	18	78.3

[a] Clinically meaningful improvement = reduction of ≥ 15 points (1SD) on the IES-R. Waiting list n = 25, Treatment n = 23. Fisher's exact test, $p < .001$.
[b] Using an IES-R cut-off score of 33 (Creamer et al., 2003). Waiting list n = 25, Treatment n = 23. Fisher's exact test, $p < .001$.
* $p < .05$; No other significant between-group difference was found among any other variables of this Table.

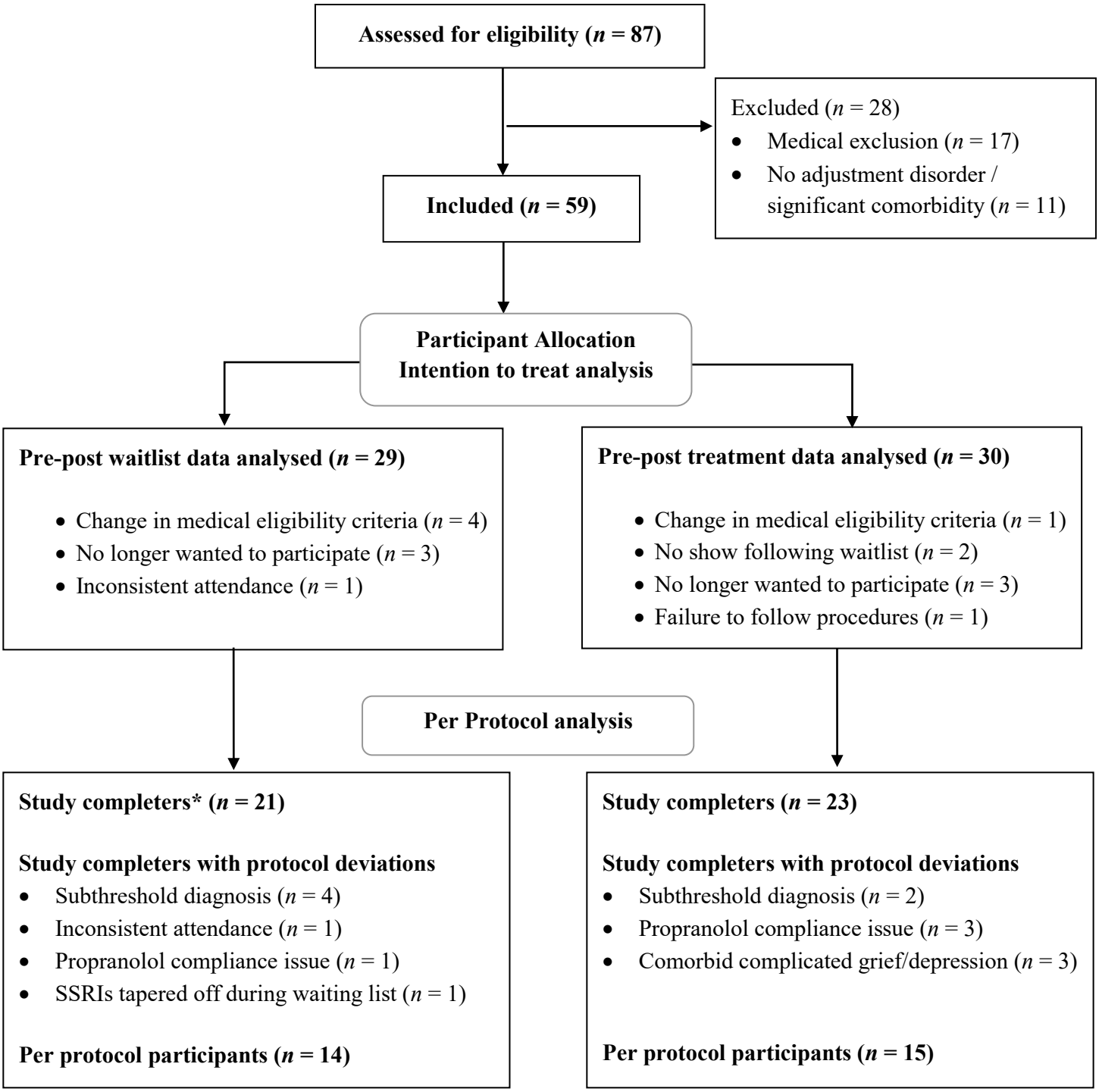

Figure 1. Flow of participants through the clinical trial. *Study completer defined as at least 4 treatments completed.

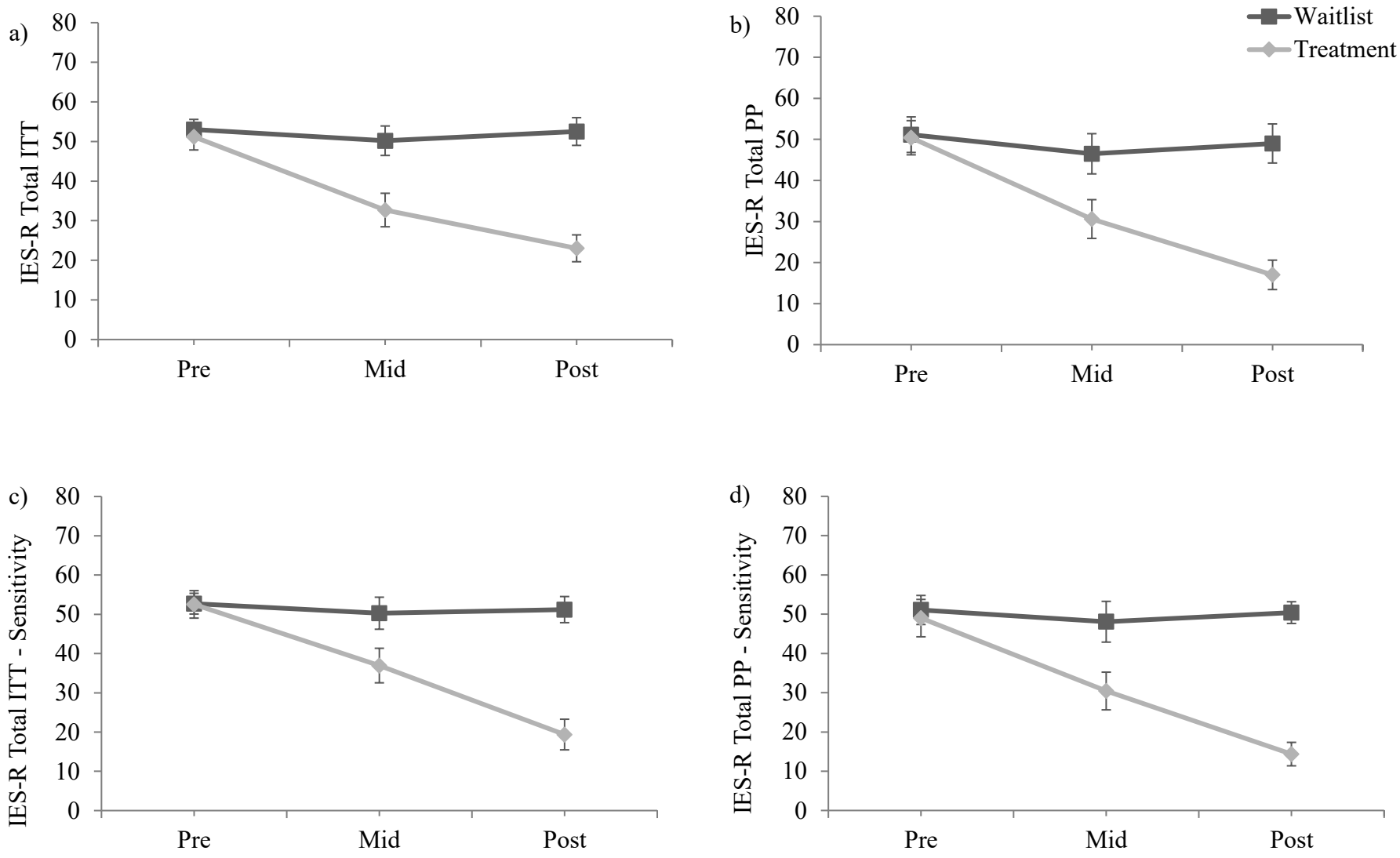

Figure 2. Mean(SE) self-report symptoms of event-related stress across a waitlist period and a reconsolidation therapy treatment period. Panels a) and b) represent results from primary analysis, and panels c) and d) represent results from sensitivity analysis.

Table 2.

Mean(SE) Event-Related Stress Symptoms by Group.

Measure	Primary ITT analysis			
	Waitlist *n* = 29		Treatment *n* = 30	
	M	*SE*	*M*	*SE*
IES-R Pre	53.03	2.55	51.19	3.33
IES-R Mid	50.20	3.72	32.70	4.23
IES-R Post	52.52	3.50	23.03	3.39
	Primary PP analysis			
	Waitlist *n* = 14		Treatment *n* = 15	
IES-R Pre	51.15	4.33	50.40	4.16
IES-R Mid	46.49	4.90	30.60	4.72
IES-R Post	49.00	4.76	17.00	3.52
	Sensitivity ITT analysis			
	Waitlist *n* = 30		Treatment *n* = 29	
IES-R Pre	52.70	2.64	52.52	3.50
IES-R Mid	50.27	4.08	36.94	4.40
IES-R Post	51.19	3.33	19.37	3.90
	Sensitivity PP analysis			
	Waitlist *n* = 15		Treatment *n* = 14	
IES-R Pre	51.07	3.70	49.00	4.76
IES-R Mid	48.07	5.19	30.43	4.80
IES-R Post	50.40	4.16	14.36	2.78

Table 3.

ANCOVA Results: Between-group Difference on Post-treatment IES-R and HSCL-25, Controlling for Baseline

Measure	*Primary analysis without covariates*					*Primary analysis with covariates*				
	F	*df*	*β*	*SE*	*95%CI*	*F*	*df*	*β*	*SE*	*95%CI*
ITT Analysis (n = 59)										
IES-R	44.98*	41.38	28.54	4.26	[20.18, 36.90]	36.57*	36.62	28.27	4.67	[19.08, 37.45]
HSCL-25	15.36*	24.46	.59	.15	[.30, .90]	12.56*	26.26	.60	.17	[.27, .93]
PP Analysis (n = 29)										
IES-R	43.61*	26	31.56	4.78	[22.20, 40.93]	27.77*	19.45	30.42	5.77	[19.11, 41.74]
HSCL-25	17.84*	26	.68	.16	[.36, .98)	11.86*	19.05	.58	.17	[.25, .91]
	Sensitivity analysis without covariates					*Sensitivity analysis with covariates*				
ITT Analysis										
IES-R	47.25*	26.96	31.81	4.63	[22.66, 40.96]	41.54*	25.99	30.89	4.79	[21.42, 40.37]
HSCL-25	22.75*	30.72	.66	.14	[.39, .86]	21.58*	25.88	.69	.15	[.40, .98]
PP Analysis										
IES-R	65.19*	26	35.09	4.35	[26.57, 43.60]	44.42*	18.82	33.50	5.03	[23.64, 43.35]
HSCL-25	43.56*	26	.72	.11	[.50, .93]	31.38*	19.10	.68	.122	[.44, .92]

Note. * $p \leq .001$. Covariates included in the model: Duration of Relationship, Treatment Expectancy, and Time Since the Event.

Table 4.

Means(SD) and Within-group Effect Sizes for IES-R and HSCL-25 Subscale Scores Over Time (n = 44).

Measure	Baseline		Post-Waiting list			Post-Treatment		
	M	*SD*	*M*	*SD*	*d*	*M*	*SD*	*d**
HSCL-25 - Depression	2.41	.59	2.45	.68	.09	1.63	.57	1.37
HSCL-25 - Anxiety	1.77	.50	1.76	.60	.02	1.25	.31	1.02
IES-R Intrusion	22.32	6.64	21.65	7.36	.13	6.67	6.20	1.91
IES-R Avoidance	16.61	6.47	16.20	6.90	.10	7.68	6.12	1.05
IES-R Hypervigilance	12.75	5.79	11.78	6.06	.22	3.23	3.38	1.52

* *Note.* Effect size *d* reflects between group difference from post-waiting list to post-treatment.

Table 5.

Means(SD) and Within-group Effect Sizes WHOQoL-Bref Domain Scores Over Time

Measure	Baseline			Post-Waiting list			Post-Treatment		
	n	*M*	*SD*	*M*	*SD*	*d*	*M*	*SD*	*d**
Physical	40	64.29	14.65	61.78	16.08	.22	73.75	16.76	.77
Psychological	40	48.75	16.29	45.42	16.26	.33	58.65	15.91	1.01
Social	39	51.71	19.04	50.64	19.81	.07	59.40	19.97	.45
Environmental	41	69.66	15.22	67.45	16.03	.25	72.48	13.55	.45

* *Note.* Effect size *d* reflects between group difference from post-waiting list to post-treatment.

Transitional text #2

The previous two manuscripts presented the methods and results of a clinical trial investigating reconsolidation therapy using propranolol as a treatment for betrayal-related adjustment disorder. Considering adjustment disorder as a stress-response syndrome that shares common features with PTSD in its clinical presentation, this intervention is based on theories of the development and maintenance of core stress-related symptoms as rooted in the pathogenic memory of a distressing event (Maercker & Lorenz, 2018; Marks et al., 2018). Consistent with this model, emerging research suggests that the experience of betrayal or social injury / deception may involve similar neurobiological mechanisms as those implicated in emotional learning (Fisher et al., 2010; Grezes et al., 2006). Accordingly, the psychological sequela stemming from romantic partner betrayal may, at least partially, be rooted in the memory of the event. The findings presented in this dissertation thus far, albeit indirectly, lend support to these notions, and suggest that romantic partner betrayal may precipitate an adjustment disorder. As demonstrated in Chapter 4, participants reported enduring and highly distressing intrusive thoughts and memories related to the event, increased arousal and vigilance, avoidance, as well as depression, anxiety, and impairments in important areas of psychosocial function. Importantly, results supported the use of reconsolidation therapy to treat betrayal-related adjustment disorder, as statistically significant and clinically meaningful reductions in event-related stress symptoms, depression, and anxiety were observed in both the intention-to-treat and per protocol samples.

Johnson et al. (2001) argue that when a negative interpersonal event perpetuated by a romantic partner undermines the sense of security and safety embedded in the romantic attachment bond, an attachment injury may occur; the resulting state of vulnerability may

provoke psychiatric symptoms consistent with a trauma-like syndrome in the offended partner. Thus, the experience of romantic partner betrayal is likely shaped by a variety of inter- and intrapersonal factors, which can be further explored via qualitative inquiries. Qualitative research elaborates on findings from quantitative studies and provides an in-depth and eclectic understanding of the lived experience and meaning of a phenomenon for an individual. To date, few published qualitative investigations have been carried out on the experience and meaning of romantic partner betrayal (Pelling & Arvay-Buchanan, 2004; Zitzman & Butler, 2009; Salavati et al., 2018). Although findings have been interpreted considering trauma theory from an etic perspective (e.g., from the perspective of the researcher or observer), no qualitative research to date has examined the extent to which the construct of trauma is a reasonable explanatory model of symptoms from an emic perspective (e.g., from the perspective of the affected individual). The following manuscript presents a qualitative investigation of the experience and meaning of romantic partner betrayal among injured individuals who had recently completed a clinical trial of reconsolidation therapy.

Chapter 5

Is romantic partner betrayal a form of traumatic experience?

"We are never so defenseless against suffering as when we love, never no helplessly unhappy as when we have lost our loved object of its love"

– Sigmund Freud, Civilization and its Discontents, 1930

Lonergan, M., Brunet, A., Rivest-Beauregard, M., & Groleau, D. Is romantic betrayal a form of traumatic experience? [Manuscript in preparation for *Journal of Counselling Psychology*].

Abstract

Background: Romantic betrayal may precipitate an adjustment disorder in some individuals, an event-related psychological disturbance that is characterized by anxiety, depression, and posttraumatic stress disorder-like symptoms of intrusions, avoidance, increased vigilance, and failure-to-adapt. Although prior qualitative work suggests that romantic partner betrayal may be experienced as a "traumatic" event, no research to date has investigated the extent to which trauma theory is a reasonable explanatory model of symptoms and treatment from the perspective of injured individuals. This research aims to address this gap.

Methods: Individual face-to-face in-depth interviews were conducted using the McGill Illness Narrative Interview with 13 participants enrolled in a clinical trial of reconsolidation therapy for event-related stress symptoms. Data was analysed using thematic content analysis.

Results: Although participants used trauma metaphors and prototypes to describe their betrayal experience, few identified their reaction as traumatic stress symptoms. Respondents attributed their symptoms to typical relationship dissolution, or burnout, yet admitted that the experience of betrayal was somehow more painful and invasive. Reframing their experience as rooted in the experience and memory of a critical life event provided participants with emotional clarity, validation, and relief that there was a brief and targeted solution.

Conclusion: The emotional memory and reconsolidation frameworks of event-related stress were perceived as a plausible explanatory model of symptoms and treatment, respectively, for the effects of romantic partner betrayal. Results support the continued investigation of the pathogenic memory model of betrayal-related adjustment disorder.

Keywords: Romantic betrayal, trauma, qualitative interview, meaning and experience, treatment

Public Significance: This qualitative study advances the notion that romantic partner betrayal can be experienced as a shocking event leading to debilitating stress-related symptoms including intrusive thoughts and memories, avoidance, negative changes in worldviews, dysphoric mood, and anxiety in some injured individuals. Further, many affected individuals may face difficulties in identifying their symptoms, which may prolong distress. Results from this study suggest that incorporating emotional memory-based theories of event-related stress symptoms and their treatment in clinical practice may improve outcome for suffering individuals.

Introduction

Given the importance of positive and secure romantic attachments to health and well-being (Lawrence, Rogers, Zajacova, & Wadsworth, 2018), it is no surprise that romantic partner betrayal (e.g., infidelity, sudden abandonment) can be a painful and devastating experience. Unfortunately, betrayals in committed relationships are common. Couple's therapists assert that betrayal is frequently encountered in practice and especially difficult to treat (Gordon, Khaddouma, Baucom, & Snyder, 2015; Whisman, Dixon, & Johnson, 1997). Rates of infidelity, for example, are approximately 25% in marital relationships and up to three times higher in non-married dating relationships (Blow & Hartnett, 2005; Fincham & May, 2017; Maddox Shaw, Rhoades, Allen, Stanley, & Markman, 2013). Such events are not only among the main reasons for relationship breakdown but are also associated with a myriad of psychological symptoms for injured individuals, such as depression, anxiety, intrusive thoughts / rumination, increased vigilance, and cognitive distortions concerning views of the self and others (Roos, Willetts, Canavello, & Bennett, 2017; Laaser, Putney, Bundick, Delmonico, & Griffin, 2017; Scott, Rhoades, Stanley, Allen, & Markman, 2013; Whisman, 2015). However, to date, little is known about the phenomenological experience of romantic betrayal, which has limited the development of individualized treatments.

The Psychological Effects of Romantic Partner Betrayal

The notion of betrayal has long been considered a critical component of psychological trauma (Akhtar, 2013; Freyd, 1996). Between romantic partners, an act of betrayal can be conceptualized as one that violates core beliefs in the relationship and the partner as a source of stability, safety, comfort, and love, particularly during times of personal distress (Johnson, Makinen, and Millikin, 2001). Such events are distinguished from the ebbs and flows of couple

relationships by their perceived threat to the security of the romantic relationship, and from posttraumatic stress disorder (PTSD)-related trauma by their lack of imminent life-threat (Johnson et al., 2001; Maercker & Lorenz, 2018). Johnson et al. (2001) argue that these 'attachment injuries' may be best understood as "trauma with a small 't'" (p. 150). Indeed, the resulting state of destabilization and vulnerability following the discovery of romantic betrayal may provoke an adjustment disorder in the injured partner. In the *Diagnostic and Statistical Manual for Mental Disorders* (*DSM-5*; American Psychiatric Association [APA], 2013), adjustment disorder is classified among the trauma- and stressor-related disorders along with PTSD.

Like PTSD, the etiology of adjustment disorder is linked to individual differences in the experience and subjective appraisal of a precipitating stressor, although in PTSD, the stressor (i.e., Criterion A.) must involve the direct or indirect threat of death, serious injury, or sexual violence (APA, 2013; Maercker & Lorenz, 2018; Glaesmer, Romppel, Brähler, Hinz, & Maercker, 2015). As a result, symptoms of adjustment disorder overlap with those associated with PTSD and include intrusive and obsessive thoughts and memories of the stressor, increased arousal to reminders, avoidance, emotional volatility, as well as depression, anxiety, and functional impairment (APA, 2013; Maercker & Lorenz, 2018; Maercker, Einsle, & Kollner, 2007). Although increasing evidence suggests that between 30% and 60% of romantically betrayed partners experience such symptoms (Laaser et al., 2017; Roos et al., 2017; Whisman, 2015), individualized treatments remain limited. However, neurobiological advances in understanding the pathophysiology of event-related distress have opened the door to innovative and promising treatment avenues (Ecker, 2018; Marks, Franklin, & Zoellner, 2018).

A Novel Treatment for Betrayal-Related Adjustment Disorder

Stressor-related syndromes can be considered the clinical expression of a pathological emotional memory of the precipitating negative life-event (Marks et al., 2018; Iyadurai, Visser, et al., 2018; Maercker & Lorenz, 2018). It is well demonstrated that emotion enhances memory; for some individuals, the emotional salience of an experience may result in persistent hypermnesia of the event (McGaugh, 2004, 2013). The memory becomes too easily (re)activated, either spontaneously or through exposure to contextual cues, resulting in the clinical expression of traumatic stress symptoms (Pitman, 1989; McGaugh, 2013; Marks et al., 2018). Reconsolidation theory posits that memory retrieval induces a transient period of lability, which is vulnerable to pharmacological interference (Elsey, Van Ast, & Kindt, 2018; Lee, Nader, & Schiller, 2017). For instance, administering the reconsolidation blocker propranolol during this period of lability dampens emotional memory enhancement, presumably by disrupting reconsolidation mechanisms (Besnard, Caboche, & Laroche, 2012; Lonergan, Olivera-Figueroa, Pitman, & Brunet, 2013). Translating this paradigm to a clinical intervention for patients with PTSD, the typical treatment protocol involves having participants take propranolol 60 minutes prior to writing or reading a detailed narrative of the index event in the first person, present tense, which serves as a retrieval cue (Brunet & Lonergan, manual in preparation). In a recent placebo-controlled clinical trial, this approach resulted in a 53% - 56% improvement in self-report symptoms of traumatic stress in patients with chronic PTSD (Brunet et al., 2018).

While our team further demonstrated that reconsolidation therapy can also reduce symptoms of depression and event-related stress to below clinical levels in close to 70% of relationally betrayed individuals (Lonergan, Saumier, et al., in preparation), the extent to which this framework is a plausible explanatory model of treatment for betrayed individuals remains

unknown. This research aims to investigate the meaning and experience of romantic partner betrayal, with a focus on the perceived acceptability of the emotional memory framework and reconsolidation therapy using propranolol as an explanatory model of symptoms and treatment, respectively. The following two research questions were posed:

- What is the meaning and experience of romantic betrayal?
- To what extent do romantically betrayed individuals identify with an emotional memory framework of event-related distress as an explanatory model of symptoms and treatment?

Method

Participants

This qualitative investigation was nested within a larger clinical trial of reconsolidation therapy using propranolol to treat enduring symptoms of distress following the discovery of betrayal[2]. Participants who completed the clinical trial and indicated on their original consent form that they agreed to be contacted for future studies (n = 43) were eligible to participate in the qualitative portion of the study, and as a result 13 accepted. All participants provided written consent to participate in the qualitative portion of the study. The research ethics board of the Douglas Mental Health University Institute approved this ancillary study (REB #17-05).

Procedures

After an average of 2.63 (SD = 2.11) months following treatment completion, participants were invited to the Douglas Research Center and interviewed for 1.5 – 2 hours using the McGill Illness Narrative Interview (MINI), a semi-structured interview used in qualitative health research that was developed by Groleau, Young, and Kirmayer (2006) to explore illness meaning and experience, pathways to care, experience of treatment, and change in worldview. The MINI contains four sections. The first section obtains a narrative of the sequence of events leading to

[2] For full details of the clinical trial's methods and treatment protocol, see Lonergan et al. (submitted).

the illness; the second uncovers illness prototypes of self and others and analogical reasoning about the illness; the third elicits an account of perceived cause of the illness and corresponding explanatory model. Explanatory models of illness reveal rational ways of reasoning about the causes of an illness, while illness prototypes provide access to emotional and analogical reasoning based on one's own prior experiences, that of others, and media representations (Groleau et al., 2006). Finally, the fourth section inquires about treatment-experience, health behavior and world view. Interviews were conducted at the Douglas Institute by the first author (M.L.), who was trained to use the MINI by the senior author (D.G.).

Instruments and Data Analysis

Severity of event-related stress symptoms was assessed with the Impact of Event Scale-Revised (IES-R; Weiss & Marmar, 1997), while depression and anxiety were assessed with the Hopkins Symptom Checklist-25 (HSCL-25; Winokur, Winokur, Rickels, & Cox, 1984). All interviews using the MINI were audio-recorded and transcribed verbatim for analysis. Thematic content analysis following the steps outlined in Fereday and Muir-Cochrane (2006) was used to analyse data from the MINI. After a familiarization period where all transcripts were carefully read and openly coded for relevant ideas and themes, transcripts were deductively coded to identify the various modes of reasoning within illness narratives (metonymic), explanatory models (causal), and prototypes (analogical). This was followed by an inductive coding phase to identify major themes within each mode of reasoning. Codes were then organized in an iterative process using conceptual maps and summary tables to generate larger emic[3] themes reflecting the complexity of the experience and meaning of romantic partner betrayal. Atlas.ti (v. 8, 2016) was the application used to support the coding and qualitative analysis process.

[3] Emic: Refers to first-order concepts – the language, or concepts used by individuals to describe their experience. Vs. Etic: Refers to second-order concepts – the language, or concepts used by the scientist or research to describe the same phenomenon (Schwandt, 2014).

Results

Description of Participants

Table 1 displays the participants' sociodemographic and pre-treatment clinical information. All participants were in heterosexual relationships. Six of the 13 participants were married for over 15 years with the offending partner (range: 15 to 40 years); these participants reported infidelity as their betrayal event (e.g., sexual, emotional, or both). Five participants were with the offending partner between 1 and 6 years prior to the event, which were also infidelity-related. The remaining two participants were with the offending between 6 and 7 months prior to the event. One reported sudden physical abandonment immediately following a miscarriage, and the other reported emotional manipulation and abandonment as their index event.

The Cycle of Deceit

Figure 1 describes the sequence of events surrounding the discovery of betrayal. Often, discovery occurred during a time of life transition, for instance, while couples were living apart, planning a trip, planning to buy a home, or over the holidays. Some participants were going through something difficult at the time of the discovery, for instance, job loss, miscarriage, or family conflict. In other cases, the injured partner identified themselves as unavailable at the time the betrayal event was happening due to work or school-related commitments. When asked to describe the events surrounding the discovery, a clear pursue-withdraw dyadic pattern between the injured and offending partner, respectively, emerged. This pattern was most clear for participants who were married or cohabitating, and a minority of participants fit stages 3-8 of this cycle as discovery was unsolicited by a third party (e.g., they were told of the betrayal by someone else) or there were no discernable signs that prompted an initial suspicion phase.

Symptoms following the discovery of betrayal. Prior to receiving reconsolidation therapy, participants were diagnosed with adjustment disorder, or other trauma-related disorder depending on the duration of the stressor and syndrome (APA, 2013), as assessed with the Mini International Neuropsychiatric Interview-v.5 (Lecrubier et al., 1997). Severity of symptoms on the IES-R was comparable to what is typically found among trauma victims suffering PTSD (e.g., Creamer, Bell, & Failla, 2003). In addition, mean scores on measures of depression and anxiety symptoms fell above cut-off values indicating clinically significant psychological distress (Mattisson, Bogren, & Horstmann, 2013) particularly for depression (see Table 1). Intrusive images and memories, preoccupation with the event, and rumination were predominant in this sample, as one participant noted:

> ***Participant:*** It's really fascinating, it hurts everywhere! Your throat hurts. You can't breathe. When you think about it you hurt… You have these really graphic images, and you can't block them, there's nothing you can do. It's in your face all the time.
>
> ***Interviewer:*** What images did you have?
>
> ***Participant:*** The images were about sex, a lot. I've seen it all in my mind…
> *[female, 44]*

> ***Participant:*** I forgot to mention before, but for me, it always comes back, I see it constantly in my head. Constantly. When I said I was distracted before, that was why! It replays like a movie all the time. For me there are several images that come back, because I had made other discoveries over time too… But the longest and biggest is that period of 24 hours. It might seem short, but for me it's long in my head… the moment I learned… pacing around all night, the phone calls the next day, speaking to my friend telling him that I am going out of my mind, crying in my office... there's 24-36 hours of hell in my head that I constantly revisit.
> *[male, 44]*

Symptoms reported by participants included various physical complaints such as gastrointestinal distress, hair loss, perceived increase in blood pressure, nose bleeds, racing heart, shaking, sweating, muscle weakness, and pronounced weight loss. Emotional and behavioral symptoms included persistent sadness and crying spells, difficulty with concentration, insomnia and nightmares, hypervigilance, avoidance, irritability and emotional volatility, loss of interest, rumination, lack of appetite, and loss of libido. Two participants had engaged in maladaptive behaviors, such as smoking or excessive drinking, for several months following discovery. Anger was predominant and persisted for many throughout the treatment phase of the study. Physiological symptoms tended to be experienced more severely in the immediate aftermath of discovery and although tapered off somewhat a few months later, tended to recur in the presence of reminder cues. Similarly, emotional and behavioral distress fluctuated but was sustained and was particularly severe when reminded of the partner, the discovery event, or the context of the betrayal. Examples of reminders or "triggers" included salient dates (e.g., "today is the day that I found out [of the betrayal] one year ago"; "on this day 6 months ago I realize now he was with her"), photographs on social media, seeing someone who looks, speaks, or walks similar to the offending partner, or hearing about the offending partner through mutual acquaintances.

The Betrayal Trauma Narrative: Explanatory Models and Prototype Reasoning

Figure 2 displays the thematic map reflecting causal factors perceived by participants for their distress associated with betrayal, which they related to three main themes: 1) suspicion, 2) the shock of discovery, and 3) the attachment significance.

Suspicion and doubt prior to discovery. Prior to the discovery of betrayal, most participants felt a 'sixth sense', or suspicion, that something was not quite right in their relationship. They described this feeling as intangible, that something was 'just off'. For some,

this suspicion phase led to pronounced psychological distress, including intense anxiety, insomnia, and a 'feeling of going crazy', which prompted clandestine behaviors such as hiring private investigators, going through social media accounts, and using cellular GPS tracking devices in search for the truth. Others claimed that they failed to see any signs, and in hindsight, may have done so purposefully because they were not ready to face the truth. For one participant, the distress associated with the suspicion phase provoked a visit with a primary care physician, who prescribed anti-anxiety medication.

The betrayal event: Shock, loss, and shattered assumptions. Discovery of betrayal was consistently experienced as an unpredictable and shocking event that precipitated an intense physiological reaction (e.g., increased heart rate, sweating, head spinning), followed by a period of denial and an urgent need to attempt to fix the relationship. However, irrespective of whether rebuilding efforts were successful, the pain of betrayal was profound and lasting, as revealed through the metaphors participants used to make sense of their experience, which often involved violent and trauma-like language (Figure 3).

> ***Participant:*** When I really knew that he had betrayed me, the pain, and the torture it was like I had been cut off at my knees, … if you want to visualize you know like some sort of monster, with big long claws, and just digging deep into your heart, ripping your heart out while you are still breathing and alive and very conscious, and taking a bite out of your heart right in front of your face, that's what it feels like. It was excruciating… excruciatingly painful.
>
> *[female, 50]*

Particularly among those who were no longer in the relationship with the offending partner, betrayal or abandonment was experienced as a significant and sudden loss, and many described their reaction as akin to grief. Participants grieved not only the death of the relationship, but also the loss of their positive perception of their partner. They readily identified

a lack of control or understanding of the situation and their reaction as a significant source of distress, especially concerning the inability to 'get out of the vicious cycle' of invasive rumination and intrusions. Although participants could logically identify reasons why the betrayal occurred, for instance, that they themselves, their partner, or their relationship was in an unstable place at the time, most continued to question and failed to emotionally understand how their partner could be so deceitful and manipulative, which prolonged distress.

Discovery of betrayal destabilized participants' sense of self, as well as their trust in their current or future partners, and the world of relationships, which underscored anger, resentment, anxiety, and depression. A sense of shame and stigma surrounding the event contributed to feelings of isolation, of feeling misunderstood by family and friends, and of feeling excessive guilt and self-blame. Regardless of whether there was a perceived intent to harm, participants were particularly affected by the realization that their partner had consciously decided to commit the act, and / or purposefully employed deceitful and manipulative tactics to minimize what they had done. Interestingly, these changes in cognitive schemas were both a cause of psychological distress and a psychological effect of the betrayal event.

> ***Participant:*** Betrayal is not an accident. It's someone who takes a knife and does this [stabbing] in your back. He betrayed me, and he is a dishonest liar... at what point he decided that he loved someone else more than me, I will never know because I saw no sign, apart from that one Sunday that he was absent. It's a terrible betrayal… It changed my life you know, it changed my life forever.
> *[female, 50]*

> ***Participant:*** Everybody sort of sees me as a very stern, rigid individual in what I do. I am quite professional in what I do, and I know how to do it. I sort of hold truth to who I am and to myself. No, this, what this did was, it got me. I had to speak to my partners about how I felt completely damaged. I'll be honest, I never would have thought that I would feel compromised to that point, to have to speak to them about it. And I've gone through

> some events, you know, people passing... but nothing… it's almost as if it really just shook who I was… or the person I had come to believe I was.
> *[male, 47]*

The attachment significance of the event: Vulnerability, caregiving, and prior attachment injuries. Prior to discovery, several respondents felt that their partner was distant and withdrawn from their relationship, and seemingly uninvolved in maintaining intimacy or the home life. When the source of the withdrawal and distance was identified as external to the relationship (e.g., work obligations), participants readily recognized the difficulties their partner was facing and attempted to provide support; such attempts were often perceived as futile. Others asserted that unbeknownst to them at the time, their partner was going through a period of depression and self-doubt; questioning their role in the relationship or questioning whether they wanted to be in the relationship. In all circumstances, the feeling of unreciprocated sharing and caring, or being kept in the dark about what their partner was experiencing, precipitated significant emotional turmoil during both the suspicion phase and post-discovery.

Seven out of thirteen participants identified that they personally, or their relationship, was going through a period of transition during the time of the discovery such as job loss, miscarriage, career transition, living apart from their partner on a part-time basis for work or school obligations, or during the holidays, which they considered contributed to the psychological impact of betrayal. Four of these participants identified being in a time of personal vulnerability, and the lack of responsiveness from their partner was especially noticeable and painful. Three participants, who were living apart from their partner, did not feel personal vulnerability yet acknowledged that their circumstances may have strained the relationship. Finally, four participants identified previous attachment-related disruptions with primary

attachment figures during childhood or early adulthood (e.g., parents, close family members) as a contributing factor to the impact of betrayal by their romantic partner.

> ***Participant:*** I know where my abandonment issues stem from.
> ***Interviewer***: Where do you think?
> ***Participant***: I was really close to an aunt when I was like from the age of 2 to 5 I guess formative years, and I spent a lot of time with her. My mom had 8 children, she wanted 4 and I was number 5. So, I think I internalize a lot of feelings about oh I wasn't wanted…. So, I bonded with her. I never felt like I had bonded with my mom…. I know that this issue of trust, this fear of abandonment, I know that's where it comes from… *[female, 44]*

Prototypes of self. Most respondents asserted that the discovery of betrayal was the most difficult event they had experienced in their lifetime. Participants tentatively related their current distress to experiences with partner-initiated relationship dissolution, divorce / separation, work-related 'burnout', depression, grief, and / or prior attachment-related issues from childhood. Past experiences of relationship dissolution occurred in relationships that were however less committed, highlighting the attachment significance of the index relationship in perpetuating post-betrayal distress. For example, after finding out that her partner in a previous relationship had engaged in an affair, one participant laughed, claiming: "I never considered that guy the love of my life". Throughout all such comparisons, the perceived inability to control the situation and feelings of victimization were considered similar to the effects of betrayal. However, betrayal was perceived as an unpredictable and vicious personal attack, which made their current experience more distressing. While some related to prior experiences with 'burnout', they asserted that their recent experience with betrayal was somehow different and more severe, largely due to the presence of panic and triggers.

> ***Participant: …***I knew it wasn't depression. Because I was able to… I was able to work, I had my appetite, I had my friends, I saw my friends, I did activities, I still danced!
> ***Interviewer:*** What did you think you were experiencing?
> ***Participant:*** I think there really was a trigger. I saw the truck with the little cat paws [the mistress's car], and it was automatic. I had to move, I couldn't drive anymore. I was at the grocery store, and when I saw her and that truck, my knees would literally buckle …
> *[female, 59]*

Prototypes of others. Some knew or suspected that someone in their family, a friend, or a work colleague had experienced betrayal, but did not openly talk about it, which contributed to the perception of betrayal as shameful and stigmatizing. The few who did know of others who had been betrayed related to feelings of sadness expressed by others; of being unable to rationalize their reactions and of being replaced by another. A minority used their experience to try and help others with their own. Two participants had sought out contact with individuals romantically involved with the offending partner, either as the 'mistress' or a new partner. Both found this experience cathartic, asserting that the 'other woman' was the only one who could truly understand their experience. Across participants, relationship dissolution not involving betrayal was considered a normal process that everyone experiences, whereas betrayal occurring in the context of marriage, particularly if children were involved, was seemingly worse, despite the emotional reactions to betrayal being perceived as similar.

> ***Participant:*** I know of somebody, yeah. A colleague of mine.
> ***Interviewer:*** How do you consider your experiences to be similar or different?
> ***Participant:*** Well, in both cases, I mean there's obviously the betrayal, you know, someone cheating. He's crushed… I see exactly in him what I saw in myself, he's all over the place. But definitely the circumstances are different, he's married, and has a child with her, she has zero respect for him or their child… So that's a big difference…
> *[male, 47]*

Prototypes of media and trauma: The researcher as a media prototype. Many participants felt as though their pain was perceived by others to be more trivial than had they experienced grief or life-threatening trauma, which contributed to feelings of shame, frustration, and isolation. They believed they could only burden their social network for a specified amount of time, after which they should have moved on. Thus, feeling as though their distress was not abating and they've exhausted their support network, many participants turned to the media, including the internet and books, to make sense of their experience and find solace. Chat rooms, blogs, and articles about divorce or separation were not generally perceived as helpful. Some participants, however, found several resources that they related to, much of which consisted of books and articles written by authors that inspired this research (e.g., Ortman, 2009; St-Père, 2012). This material validated participants experience by reframing betrayal using a trauma perspective, although at the time most had not used that idiom. Furthermore, no participant was aware of any individualized treatment specifically targeted toward the effects of betrayal.

Similar to their experience, psychological trauma was perceived by participants to be something that alters an individuals' sense of self and involves a vicious cycle of 'flashbacks' and 'triggers', or a mental state that is inescapable. Participants drew parallels between their experience with betrayal and their perception of PTSD-related trauma. Here, the inability to control the event or the emotional response, as well as symptoms of intrusions, re-experiencing, and increased vigilance, were relatable. Respondents generally viewed negative interpersonal events perpetuated by someone close as somehow different and conceivably more damaging compared to those perpetuated by strangers or non-interpersonal events. One participant who had firmly labeled their reaction to sudden abandonment as traumatic loss readily identified with a family member who had experienced sudden death of a loved one. However, participants were

cautious about applying the 'trauma' label to their symptoms and experience. Trauma and PTSD were perceived as being related to life-threatening events, such as war, physical assault, disasters, or acts of terrorism, and many respondents felt that their experience was likely less severe due to the lack of violence involved. Despite acknowledging similarities, when directly asked if they had considered their reaction as akin to trauma, almost all participants said no.

> ***Interviewer:*** Had you considered that you were experiencing a traumatic reaction?
> ***Participant:*** No.
> ***Interviewer:*** Do you know anyone who has experienced trauma, whether it was related to betrayal or something else?
> ***Participant:*** Well, you know, in Lac-Mégantic, the whole town was traumatized. They were talking a lot about resilience because it was a huge collective trauma. A train arrived in the middle of the town and 47 people died. It's incredible, and very traumatizing... I've told him [husband] in the past, this … for me, this is my train.
> *[female, 44]*

Some participants were hesitant about contacting the research team for information about the clinical trial. Although they felt like their pain would never end, they wondered if their case was 'bad enough' to warrant any specific intervention. Others felt skeptical of the simplicity of the treatment approach. Nevertheless, after being exposed to media representations of our research, almost all participants felt a sense of insight and validation of their experience (see Appendix F). The emotional memory framework of the development of event-related distress provided participants with an explanation for their experience. This model not only framed their symptoms as neurobiologically based in the memory of a critical life-event, but also offered a specific solution: reduce the embodied salience of the memory, and the symptoms will dissipate. This is exemplified by one participant who had seen a documentary on our team's work on PTSD related to the November 2015 terror attacks in Paris.

> ***Participant***: I already knew it [the treatment] was for me when I heard you on the radio because I had seen the other program on the Bataclan. When I saw the treatment that was being offered to the traumatized people in the Bataclan, I thought, Oh My God! That's it! The more I listened, the more I thought that this applied so much to me! I didn't see anyone die, but it would still apply to me. You hurt so much that you want to forget what happened, loosen it up, take some of the weight off so that it's not always in your head… I thought, why isn't it being offered here, not only for dramas of blood, but also dramas of the heart, dramas that affect you where you can no longer function? …Then, two weeks later I heard you on *Médium Large* [radio show discussing the research], and then I was like Oh My God! You know, when you hear angels, ahhh?!
> *[female, 50]*

Participants were comforted by the fact that an academic clinical research team was investigating treatments for the enduring effects of betrayal. Some expressed concern about 'digging up old wounds', given that they had previously talked about the event only superficially. The predominant opinion was that the event constantly replayed in the mind regardless, and so the opportunity to confront it in a therapeutic context without the sense of being a burden was welcome. They further appreciated that the sessions only focused on the index event, and the role of the therapist was limited to facilitating the emotional connection to the narrative during the reading exercise without judgement or pity. However, some felt that confronting the betrayal event was a difficult experience, particularly at the beginning of the therapeutic process.

Discussion

Nested within a clinical trial investigating reconsolidation therapy to treat adjustment disorder stemming from romantic betrayal, the goal of this qualitative study was to further examine the experience and meaning of romantic betrayal and its treatment. Replicating prior qualitative work (Pelling & Arvay-Buchanan, 2004; Zitzman & Butler, 2009; Salavati, Mootabi,

& Sadeghi, 2018), the discovery of betrayal was experienced as a shocking event that threatened the sense of self and the belief that the romantic partner is a source of stability, safety, love, and acceptance. Participants experienced various stressor-related symptoms, including intrusions, re-experiencing, avoidance, increased vigilance, negative changes in perceptions of the self and others, as well as depression and anxiety. Despite engaging in attempts to recover (e.g., psychotherapy, anti-depressants, or anxiolytics), as well as seeking support through friends, family members, or online, symptoms persisted for months to years in some, suggesting that the consequences of romantic betrayal for injured individuals can, in some instances, be severe and enduring.

This study was the first to investigate the extent to which betrayal is a form of traumatic experience from an emic perspective. Although participants used trauma metaphors (i.e. "I felt like I was shell-shocked") and prototypes (i.e., comparison to man-made disaster in Lac-Mégantic) to reason about their distress, when directly asked if they believed they had experienced a traumatic stress reaction, most said no, as they primarily related trauma to war, combat, disasters, or sexual and physical violence. Further, our findings suggest that romantically betrayed individuals may face some difficulties in labeling their emotional and behavioral symptoms, which may complicate recovery (Vine & Aldao, 2014). Finally, no participant had encountered any treatment specifically targeted for the effects of betrayal until they were exposed to media representations of the clinical trial involving reconsolidation therapy. The treatment they were proposed offered a framework for understanding betrayal-related distress as rooted in the emotional memory of a critical life-event, which provided participants with insight that was followed by a sense of acceptance, validation, and relief that there was a solution to their distress.

Theoretical Implications: Shattered Assumptions and Intrusive Memories

In line with prior work (Pelling & Arvay-Buchanan, 2004; Zitzman & Butler, 2009), findings from this study can be interpreted in light of the conceptual overlap between cognitive theories of PTSD and attachment theory, which postulate that posttraumatic pathology can arise after exposure to events that challenge fundamental assumptions of safety and trust in the self, others, and the world (Bowlby, 1969, 1973; Charuvastra & Cloitre, 2008; Brewin & Holmes, 2003; Ehlers & Clark, 2000). Following a traumatic experience, the previously safe and predictable world becomes dangerous and uncontrollable, others become deceitful and ill-intentioned, and the self is no longer perceived as valuable, competent, and worthy (Janoff-Bulman, 1989; Brewin & Holmes, 2003). According to attachment theory, this negative shift in cognitive schema is particularly pronounced if the distressing event involves betrayal or abandonment by a primary attachment figure; an individual on whom one relies on for safety, comfort, and caring during times of need, such as a parent or romantic partner (Bowlby, 1973; Bernstein & Freyd, 2014). Such cognitive distortions underlie an inability to reconstruct a coherent view of the self and others, leading to an enduring sense of threat and debilitating symptoms of intrusive images and memories, re-experiencing, avoidance, and increased vigilance (Ehlers' & Clark, 2000).

Building on these central concepts, Johnson et al. (2001) argue that an attachment injury can occur in the context of romantic relationships "when one partner violates the assumption that the other will offer comfort and caring in times of danger or distress" (p. 145). The event becomes a crucial moment that fundamentally alters the relationship dynamics, resulting in a pursue-withdraw dyadic pattern that leads to significant relationship distress, and in many cases, relationship breakdown (see also Figure 1). The finding that participants were often in a time of

transition or vulnerability (e.g., job loss, miscarriage, living apart) during discovery suggests that attachment needs may have activated, and the resulting impact of betrayal more profound. Further, the suspicion phase, the discovery event, and the subsequent emotional and behavioral symptoms were consistently experienced as unpredictable, uncontrollable, and incomprehensible. In the aftermath of discovery, participants identified a negative change in cognitive schemas of the self, the partner, and the world of relationships as both a cause and consequence of their distress. In addition, participants reported enduring anger, shame, guilt, and humiliation, which are prominent in the phenomenological experience of traumatic stress and consistent with a negative shift in worldviews (Brewin & Holmes, 2003; Zitzman & Butler, 2009). In this sample, the inability to reconcile a negative change in their perception of their partner and sense of self prolonged intrusions, ruminations, and overall psychological distress.

The theories of PTSD discussed above form the basis of Maercker et al.'s (2007) framework of adjustment disorder as a stress-related syndrome that can occur following a non-life-threatening event, such as job loss, divorce, persistent marital problems, or as suggested here, romantic partner betrayal (see also Horowitz, 1986; Maercker & Lorenz, 2018). According to Maercker and Lorenz (2018), the etiology of adjustment disorder involves a dysfunction in memory mechanisms and individual differences regarding psychosocial and personality factors. Indeed, intrusive memories, preoccupations, and / or re-experiencing can result from exposure to various forms of painful or traumatic life events and are considered a transdiagnostic symptom that underlies a range of psychological disorders when persistent and distressing (Marks et al., 2018; Mihailova & Jobson, 2018; O'Toole, Watson, Rosenberg, & Bernsten, 2016; Brewin, Gregory, Lipton, & Burgess, 2010; Maercker & Lorenz, 2018). Importantly, a distinction has been made in the literature concerning the source of intrusions, which may stem from

autobiographical memories of past distressing experiences, or from hypothetical situations and outcomes; both forms can be enduring and debilitating and often co-occur (Marks et al., 2018; Brewin et al., 2010). Consistent with these views, intrusions and preoccupation symptoms were notable in this sample and considered by participants to be among the most difficult and distressing aspect of their experience. Further, intrusions and re-experiencing symptoms reflected not only the autobiographical memory of the discovery event, but also imagined scenarios (e.g., sexual) regarding the context of the offending partner's betrayal.

However, our findings reflect a paradox that participants were facing; although they recognized this similarity between their experience and that of PTSD, they did not relate their experience to traumatic stress. Most struggled to fully understand their symptoms, and subsequently entered a state of confusion and desperation, which not only contributed to their distress, but may have also impeded recovery. Vine and Aldao (2014) argue that the inability to identify one's emotional states contributes to various forms of psychopathology, and further suggest that emotional labeling is a crucial step in promoting emotional regulation. Participants in this study were offered a framework that considered post-betrayal distress as stemming from the emotional memory of a critical life-event, and for which there was a targeted solution. This provided them with a sense of acceptance and relief, which likely contributed to a sense of emotional clarity. Taken together, our findings have clear and important clinical implications.

Clinical Implications: Reconsolidation Therapy as a Clinical Tool

Relationship distress is among the most common reasons for seeking mental health services, and betrayal events are among the main causes for relationship breakdown (Amato & Previti, 2003; Scott et al., 2013; Snyder & Halford, 2012). As a result, mental health professionals may be frequently faced with betrayal-injured individuals in clinical practice.

However, couple's therapists assert that betrayal events are exceedingly difficult to treat, and often represent a barrier to the effectiveness of interventions (Gordon et al., 2015; Johnson et al., 2001; Whisman et al., 1997). In this study, most participants had attempted various interventions, including individual psychotherapy, couple's therapy, or pharmacotherapy. Except for anxiolytics, which helped some participants manage insomnia, other interventions were not generally perceived as helpful for the short-term for the management of more acute distress. Considering that reconsolidation therapy is designed to target core symptoms associated with a pathogenic memory, it is possible that offering reconsolidation therapy as an adjunct treatment would increase the effectiveness of other individualized or dyadic forms of therapy. Although future research via larger clinical trials or reconsolidation therapy are needed to investigate this question, some researchers suggest that treating core event-related stress symptoms may help prevent the development of more severe pathology (Marks et al., 2018; Zelviene, & Kazlauskas, 2018).

Psychoeducational approaches that provide a framework of the development and treatment of post-betrayal distress as rooted in the emotional memory of a critical life event may help affected clients make sense of their reaction. Reconsolidation therapy using propranolol is a brief, low-cost intervention that can be easily learned by a variety of mental health professionals, and as such this therapy offers a useful tool to incorporate into clinical practice. Our results further suggest that although clients may be somewhat hesitant or skeptical about the approach, it is generally perceived as a positive and helpful experience. Side effects of the medication were considered tolerable. Although the event-exposure exercise was considered difficult, it was not deterring, improved over time, and in hindsight was felt as being necessary and welcome. Finally, the brevity of the duration of the sessions, as well as the limited number of weekly visits,

were motivating factors for treatment initiation and completion (details on how to obtain the treatment manual can be obtained from the first author).

Limitations

Some limitations of the current investigation should be noted. First, participants were purposefully recruited from a pool of individuals who had previously completed a clinical trial of reconsolidation therapy, and for the most part, were successfully treated (Lonergan et al., in preparation). Additionally, all participants were in heterosexual relationships, and while attempts were made to recruit as many men and women, more women participated in both the larger trial and the qualitative interview. Participants were predominantly well-educated Caucasian individuals with relatively stable incomes, and most betrayal events were infidelity-related. Future studies would benefit from including more diverse samples (i.e. same sex couples, queer or adolescent relationships) who may or may not have received mental health services to examine the extent to which our findings are generalizable. Second, the concept of betrayal is arguably difficult to operationalize, and similar to the construct of trauma (Young, 1997; Suarez, 2016), may vary as a function of social and cultural contexts. Future work in this area may wish to examine the degree to which our findings extend to other cultures, such as those that tolerate or adopt polygamy as a traditional practice, or to conjugal relationships that openly consent to non-monogamy. Third, this study did not focus on perceived factors related to outcome. As suggested by our findings, future research may wish to examine whether prior attachment disruptions in childhood influence the complexity of the distress following the discovery of romantic betrayal, which may have differential treatment implications.

Conclusion

Findings from this study add considerably to the literature on the effects of romantic partner betrayal in committed monogamous relationships. We found that romantic partner betrayal can be experienced as a critical life event that may precipitate an adjustment disorder. Importantly, however, some injured individuals might have trouble understanding their experience. Offering an explanatory model of symptoms and treatment based on an event-related memory framework offered insight and validated participants' experience, in addition to providing relief that their syndrome can be treated in a timely manner. Results from this study inform not only future research, but also clinical practices servicing an array of individuals affected by the devastating effects of romantic partner betrayal.

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Table 1.

Sociodemographic and Clinical Variables at Pre-Treatment

Characteristic	*M*	*SD*
Age (years)	42.23	8.41
Formal education (years)	17.62	2.50
Time since index event (years)	1.87	2.16
Severity of event-related stress symptoms at pre-treatment		
IES-R Total	50.92	13.74
IES-R Intrusion	22.92	6.75
IES-R Avoidance	16.23	5.90
IES-R Hyperarousal	11.77	5.12
Severity of psychological distress at pre-treatment		
HSCL-25 Total	1.97	.45
HSCL-25 Depression	2.21	.52
HSCL-25 Anxiety	1.60	.48
	N	*%*
Gender (% Female)	11	84.6
Annual income (Can$ ≥ 50k)	8	61.5
Remained with offending partner	5	38.4
Married / Co-habitation	4	80.0
In a relationship	1	20.0
No longer in relationship with offending partner	8	61.5
In a new relationship	4	50.0

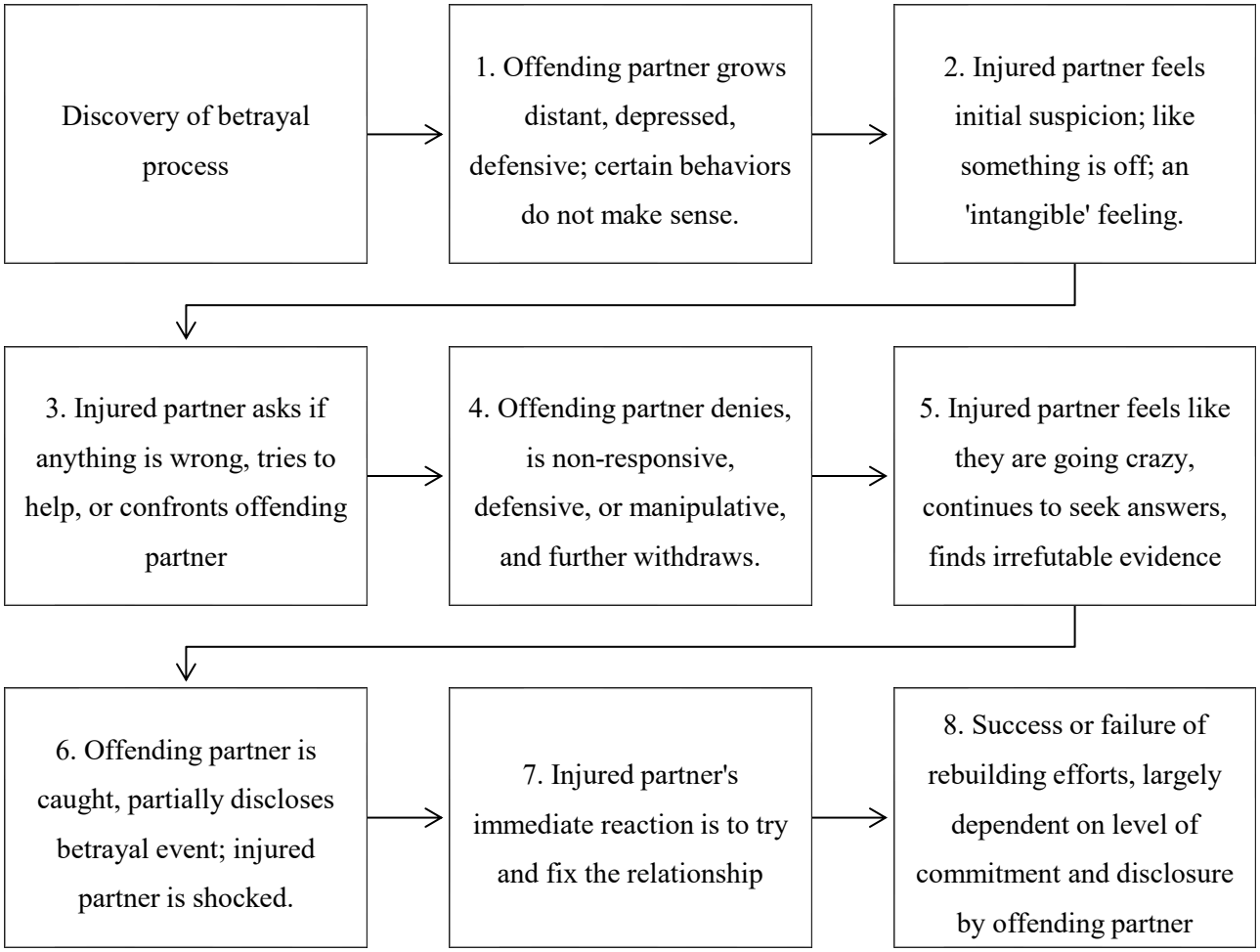

Figure 1. The cycle of deceit.

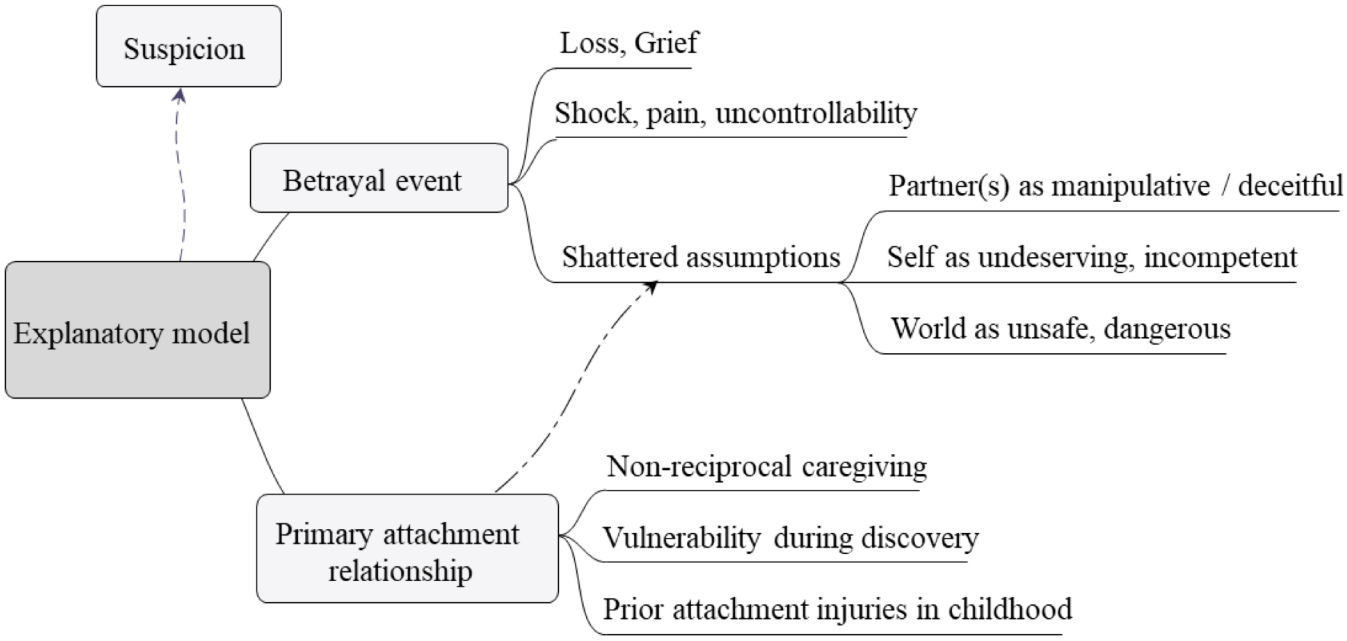

Figure 2. Causal factors for the psychological effects of romantic partner betrayal.

Figure 3. Word cloud[4]: Frequency of language used to describe betrayal

[4] A word cloud is an image of words used in a text, in which the size of each word indicates its frequency and / or importance.

Chapter 6: General Conclusion and Future Directions

Intimate relationship distress is consistently associated with physical, behavioral, and emotional disturbances (Foran et al., 2015). The profound sense of existential destabilization and vulnerability that follows the discovery of romantic partner betrayal can exacerbate relationship dysfunction and may provoke an enduring stressor-related adjustment disorder in certain individuals (APA, 2013; Johnson et al., 2001; Roos et al., 2017; Whisman, 2015). The overarching conceptual framework of this dissertation proposed that similar to PTSD, the core clinical features of betrayal-related adjustment disorder may reflect the expression of a pathogenic memory of this painful life experience, and therefore, may be treated in a similar way (Maercker & Lorenz, 2018). Reconsolidation therapy is a brief and targeted intervention based on neurobiological evidence that under certain conditions, the retrieval of a consolidated emotional memory induces a transient period of lability, during which time its salience can be inhibited by the adrenergic receptor blocker propranolol (Lee et al., 2017), resulting in a reduction of event-related stress symptoms (e.g., Brunet et al., 2018). This approach is becoming an increasingly popular method for the treatment of a variety of psychiatric syndromes rooted in pathogenic emotional memories (Ecker, 2018; Elsey et al., 2018). The three manuscripts presented in this dissertation aimed to investigate the effectiveness and perceptions of reconsolidation therapy under propranolol as a treatment for adjustment disorder stemming from romantic partner betrayal.

In the first manuscript (Chapter 3), the treatment protocol for reconsolidation therapy was disseminated, and a method for examining its effectiveness was proposed. This manuscript not only has clear implications for mental health professionals who wish to incorporate this method into their practice, but also for researchers interested in conducting larger replication studies of reconsolidation therapy or other clinical trials employing waitlist-controlled designs. Several

authors have pointed out that extraneous factors inherent in the differential treatment of participants in waitlist-controlled trials may contribute to variability in outcome (Cunningham et al., 2013; Mohr et al., 2009). Chapter 3 presented a research design that potentially reduced this threat to internal validity by treating all participants in a similar manner. The results from this investigation (Chapter 4) demonstrated that reconsolidation therapy produced statistically significant and clinically meaningful treatment effects when compared to the waitlist condition. In both the intention-to-treat and per protocol samples, significant reductions in event-related stress symptoms, as well as general psychological distress including symptoms of depression and anxiety, were observed, even after controlling for treatment expectancy, time since the event, and duration of the relationship. This research was broadened via a qualitative investigation of the experience and meaning of romantic betrayal (Chapter 5). Results demonstrated that the emotional memory and reconsolidation frameworks of event-related distress provided enlightening explanatory models of symptoms and treatment, respectively, for betrayed individuals.

The research comprised in this dissertation has important theoretical and clinical implications. Despite being the oldest recognized stressor-related disturbance, with its initial inclusion in the *DSM-I* (APA, 1952) under 'transient situational personality disorder', the diagnostic validity of adjustment disorder has been historically questioned; it is often perceived to be a subthreshold 'waste-basket' condition (Zelviene & Kazlauskas, 2018). Critics of the construct argue that its diagnostic criteria are vague, clinically impractical, and pathologizes or medicalizes normal reactions to negative life events, which may result in over-diagnosis and increased burden on health care or legal systems (Casey, 2014; Patra & Sarkar, 2013; Zelviene & Kazlauskas, 2018). However, recognizing the role of stressful life events in the etiology of

psychological dysfunction, adjustment disorder remains among the most widely used diagnoses in clinical settings (Evans et al., 2013; Maercker & Lorenz, 2018). Several authors have pointed to its usefulness in identifying and treating individuals suffering from event-based mental states who do not neatly fit into other diagnostic categories (O'Donnell et al., 2018; Zelviene & Kazlauskas, 2018). Further, the recent reconceptualization of adjustment disorder as a stress-response syndrome with clearer symptom criteria in the *ICD-11* will likely spawn a new wave of interest and research into the epidemiology, etiology, and treatment of adjustment disorder (WHO, 2018; Maercker & Lorenz, 2018). The analogy by Zelviene & Kazlauskas (2018) articulately illustrates the clinical importance of adjustment disorder as a diagnostic entity:

> AjD [adjustment disorder] could be understood by using an analogy of "flu", which is characterized as an infectious respiratory system disease caused by influenza virus. The "flu" is diagnosed through symptoms, such as fever, cough, and headache among others. The majority of patients recover; however, some individuals may develop serious complications because of the flu. AjD, in this analogy, could be assumed as a sort of "mental flu"… Health care services for individuals diagnosed with AjD should be provided in order to avoid serious complications and other mental disorders in the future. (p. 379).

It is important to consider that romantic partner betrayal should be differentiated from the more ordinary peaks and valleys of romantic relationships, or even general relationship distress and non-mutual dissolution. Consistent with Johnson et al.'s (2001) construct of attachment injury, romantic partner betrayal involves a deep violation of trust and expectations; a wound in the attachment relationship caused by the deceptive or neglectful actions of one partner toward the other that may not always involve a direct intent-to-harm, but may still be perceived in such a

way and often occurs during a time of vulnerability. While most individuals will recover from such events with time and support, a minority may not. This idea also aligns with research on trauma and PTSD; while up to 90% of individuals will be exposed to a Criterion A traumatic event in their lifetime, only a minority develop PTSD (Kilpatrick et al., 2013). Thus, among the objectives of this dissertation was to draw attention to the notion that for some individuals, discovering they have been betrayed by a trusted life-partner can be so devastating that they experience an enduring event-related stress syndrome, such as adjustment disorder, which can benefit from a targeted intervention.

Results from this research lend support to the conceptualization of adjustment disorder as a stress-response syndrome characterized by intrusions / preoccupations and difficulties adapting to a critical life event that was proposed by Maercker et al. (2007), and adopted in the *ICD-11* (WHO, 2018; Maercker & Lorenz, 2018). Betrayed participants in this study reported event-related stress symptoms, as well as depression, anxiety, and impairments in certain domains of quality of life, at comparable levels to other clinical populations (Mattisson, Bogren, & Horstmann, 2013; Rash et al., 2008; Skevington, Lofty, & Connel, 2004). As further highlighted in Chapter 5, negative changes in worldviews of the self, of current and future romantic partners, as well as the world of relationships were expressed by participants as both a consequence of betrayal and a cause of their distress. Additionally, Chapter 4 revealed that time since the event and duration of the relationship were not consistently correlated with baseline symptom severity. These findings suggest that adjustment disorder may not only be more enduring than previously thought (Maercker et al., 2012), but also that additional influences, such as the attachment significance of the relationship, may be important determinants of the negative effects of romantic betrayal (Johnson et al., 2001). This notion is supported by results of the qualitative

investigation, which revealed that the level of attachment felt toward the offending partner was perceived by participants as being an important factor for the psychological distress following the discovery of betrayal. An additional intriguing finding from Chapter 5 was that betrayed individuals may express difficulty understanding their emotional reaction, which may have perpetuated symptom chronicity.

Taken together, findings from this research suggest that in some instances, romantic betrayal may lead to enduring psychological symptoms that are consistent with an adjustment disorder and rooted in the experience of the betrayal event, yet the emotional disturbance may not be entirely comprehensible to injured individuals. Incorporating an emotional memory framework of event-related distress and reconsolidation therapy as an explanatory model of symptoms and treatment, respectively, into clinical practice may improve outcome for suffering individuals. Importantly, however, the results also highlight the need for epidemiological studies employing a structured framework of adjustment disorder, as well as additional exploration of betrayal events as a precipitating stressor, as this research did not directly examine the validity of adjustment disorder as a diagnostic construct in this population. Such inquiries will make substantial contributions to the advancement of knowledge concerning the diagnosis and treatment of emotional disturbances precipitated by stressful life events.

A key strength of the research that comprises this dissertation is the use of mixed methods. Integrating findings from both quantitative and qualitative research designs provided a more eclectic and in-depth understanding of the experience, meaning, and treatment of the psychological distress resulting from romantic partner betrayal. Nevertheless, there are several limitations of this research, some of which have been previously discussed in Chapters 4 and 5: i) the lack of a placebo-control, or a propranolol plus no reactivation comparator, ii) the use of

self-report measures as main clinical outcomes, and iii) generalizability issues. Future randomized trials employing a range of controls in larger and more diverse samples and including clinician-administered measures of treatment outcome are needed to substantiate (or refute) our findings. In addition, there are other issues that this research did not address, which could be elaborated in future work. First, the underlying mechanism by which reconsolidation therapy exerted its therapeutic benefit was not examined. Thus, it is not possible to definitively conclude that treatment effects were entirely due to reconsolidation impairment. Further, although substantial advances in understanding the neuroplasticity of emotional memory and its role in the development, maintenance, and treatment of event-related distress has been made in recent years (Beckers & Kindt, 2017; Ecker, 2018; Lee et al., 2017), additional experimental research is required to enlighten the underlying neural circuitry of the overlapping pathways between social or romantic betrayal and emotional memory. Second, this research did not explicitly address predictors of treatment outcome. Future research focused on investigating the conditions under which reconsolidation therapy is most effective is needed.

Betrayal, whether perpetuated by a friend, a lover, a family member, an employer, or an institution, is an important component of psychological trauma, and its devastating effects in the context of romantic relationships are being increasingly recognized (Akhtar, 2013; Anders et al., 2011; Anders et al., 2012; Johnson et al., 2001). The research presented in this dissertation represents the first investigation into expanding the use of reconsolidation therapy using propranolol to event-based stress disorders beyond PTSD. It is hoped that this thesis elucidates the psychological effects of romantic partner betrayal, ignites academic interest in examining the etiology and treatment of an importantly prevalent stress-related disorder, and provides clinicians with a valuable therapeutic tool that has the potential to help countless suffering individuals.

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APPENDICES

Appendix A. SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	__Title Page_
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	__Abstract__
	2b	All items from the World Health Organization Trial Registration Data Set	___N/A_____
Protocol version	3	Date and version identifier	_2018.17.08, V8_
Funding	4	Sources and types of financial, material, and other support	_Declarations_
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	_Declarations_
	5b	Name and contact information for the trial sponsor	__Title Page_
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	_Declarations__

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	41
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	31-34
	6b	Explanation for choice of comparators	35
Objectives	7	Specific objectives or hypotheses	34
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	35
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	36
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	36-37
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	37-38
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	38, 41

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	____37-38_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	____37-38_____
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	___38-40_____
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	__38-40; Table 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	__42_____
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	__36_____

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	__34_____
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	__35_____

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	__35_____
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	__35_____
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	__N/A_____
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	__41-42_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	___41_____
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	___41_____
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	__41-42_____
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	__41-42__
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	__41-42____

Methods: Monitoring

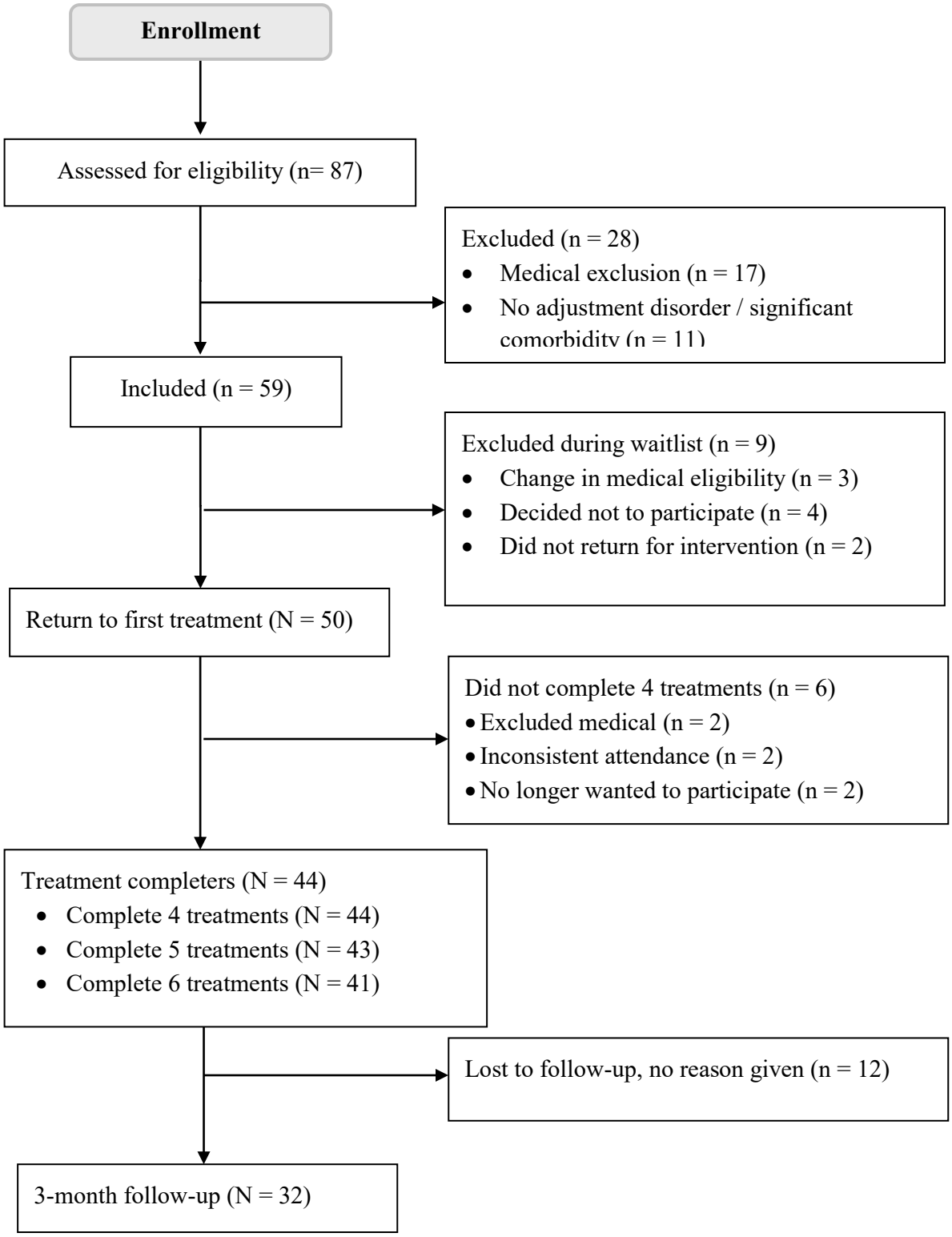
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	____41_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	___N/A_____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	___38_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	____N/A_____

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	__Declarations_
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	____41_____
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	____35_____
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	____N/A_____

Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	____41_____
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	__Declarations__
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	__ Declarations
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	___37, 41_____
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	____43_____
	31b	Authorship eligibility guidelines and any intended use of professional writers	____N/A_____
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	__Declarations__
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	_Available upon request _
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	___N/A_____

Appendix B.



Supplementary Figure 1. Participant enrollment throughout the trial.

Appendix C. Supplementary Table 1.

Primary ITT Analysis: Correlations Between Covariates and Outcomes by Group

Waitlist (N = 29)	Time Since Event	CEQ Expectancy	IES-R Pre	HSCL-25 Pre	IES-R post	HSCL-25 post
Duration of relationship	.34	.26	.04	-.06	.27	.17
Time Since Event		-.09	.01	-.21	.29	.15
CEQ Expectancy			.07	-.17	.17	-.22
IES-R Pre				.38*	.69**	.43*
HSCL-25 Pre					.18	.64**
IES-R Post						.51*

Treatment (N = 30)	Time Since Event	CEQ Expectancy	IES-R Pre	HSCL-25 Pre	IES-R post	HSCL-25 post
Duration of relationship	-.02	.29	.47*	.33	-.13	-.23
Time Since Event		-.38	.05	-.01	.12	.22
CEQ Expectancy			.12	-.11	-.24	.36
IES-R Pre				.60*	.36	.24
HSCL-25 Pre					.34	.51*
IES-R Post						.74**

Note: *$p \leq .05$, **$p < .01$

Appendix D. Supplementary Results: Sensitivity Analyses from Chapter 4

To examine the stability of our initial findings, we conducted a sensitivity analysis, which involved reversing group allocation and comparing post-waiting list data from 30 participants to post-treatment data from 29 participants. Supplementary Table 2 presents the correlations between the covariates and dependent variables, the IES-R and HSCL-25, by group. There was no evidence of collinearity between the covariates, within each level of group (*r*s < .60) and no significant between group differences on any covariate. All ANCOVA assumptions were met.

Effects of treatment on self-report symptom measures. Figure 2 panels c) & d) and Tables 2 and 3 display the results obtained from the sensitivity ANCOVA analysis on post-treatment IES-R scores, controlling for baseline (Chapter 4). Results revealed a significant between-group difference on post-treatment IES-R scores ($p < .001$, $d = 1.62$). The pre-post effect size for the waitlist condition was $d = .12$, while the pre-post effect size for the treatment condition was $d = 1.44$. Similar results were obtained in the PP sample ($p < .001$, $d = 2.64$). The pre-post effect size for the waitlist condition was $d = .07$, while the pre-post effect size for the treatment condition was $d = 2.00$. Further, there was a significant between-group difference on post-treatment HSCL-25 scores ($p < .001$; Waitlist: $M = 2.32$, $SE = .12$, Treatment $M = 1.60$, $SE = .12$, $d = 1.13$). The within group effect size for the waitlist group was $d = .05$, and for the treatment group was $d = 1.00$. Similar results were obtained in the PP analysis ($p < .001$; Waitlist: $M = 2.18$, $SE = .15$, Treatment $M = 1.37$, $SE = .08$, $d = 1.78$). The within group effect size for the waitlist group was $d = .12$, and for the treatment group was $d = 1.67$. Adding duration of relationship, time since the event, and treatment expectancy did not change the results (see Table 3, Chapter 4).

Appendix E. Supplementary Table 2.

Sensitivity ITT analysis: Correlations Between Covariates and Outcomes by Group

Waitlist N = 30	Time Since Event	CEQ Expectancy	IES-R Pre	HSCL-25 Pre	IES-R post	HSCL-25 post
Duration of relationship	-.02	.29	.33	.12	.46*	.33
Time Since Event		-.38	-.12	-.02	.05	-.01
CEQ Expectancy			.01	-.12	.12	-.11
IES-R Pre				.67**	.69**	.67**
HSCL-25 Pre					.51*	.75**
IES-R Post						.60*
Treatment N = 29	Time Since Event	CEQ Expectancy	IES-R Pre	HSCL-25 Pre	IES-R post	HSCL-25 post
Duration of relationship	.34	.26	.27	.17	-.05	-.03
Time Since Event		-.10	.29	.15	.10	.20
CEQ Expectancy			.17	-.22	-.09	-.33
IES-R Pre				.51*	.36	.26
HSCL-25 Pre					.34	.59**
IES-R Post						.74**

Note. *$p \leq .05$, **$p < .01$

Appendix F. List of Media Representations of Current Research

- Le Monde d'URBANIA. (Canada). Les pires histoires de rupture. December 2017. Podcast.
- Estelle. (Canada, France). Le propranolol : Un médicament pour réduire le chagrin lié une trahison amoureuse? 01Amour.com. July 9th, 2017. Article.
- Castigliego, G., journalist. Il Sole 24 Ore (Italy). La consapevolezza dell'attimo. July 9th, 2017. Article.
- Schetrit, N., journaliste. Paris Match (France). Quand la science soigne les peines de cœur. July 5th, 2017. Article.
- Hall, N., journalist. CJAD (Canada), The Leslie Roberts Show. Can medication help you get over a bad breakup or betrayal? July 5th, 2017. Radio Interview.
- La Rédac., journaliste. Le Bonbon (France). Un médicament pour soigner les cœurs brisés. July 4th, 2017. Article.
- Scali, D., journaliste. Journal de Montréal (Canada). Un médicament pour guérir d'une trahison amoureuse. July 1st, 2017. Article.
- Scali, D. journaliste. TVA Nouvelles (Canada). Un médicament pour guérir d'une trahison amoureuse. July 1st, 2017. TV news feature.
- Palazzo, S., journalist. Ilsussidiario (Italy). Farmaco per il mal d'amore / Il trauma post rottura può essere superato scientificamente : Il metodo. July 1st, 2017. Article.
- Magictr. journalist. The Sherbrooke Times (Canada). A drug to cure a betrayal in love. July 1st, 2017. Article.
- Leroux, J., journaliste. Radins.com (Canada). Un médicament pour soigner une rupture amoureuse. June 30th, 2017. Article.
- Sclaunich, di G., journalist. La ventisettesima ora (Italy). Ecco come noi ricercatori curiamo il mal d'amore. June 30th, 2017. Article.
- Erondel, B., journaliste. Madame Figaro (France). Un médicament pourrait-il soulager la douleur des ruptures amoureuses? June 28th, 2017. Article.
- Riou-Milliot, S., journaliste. Sciences et Avenir (France). De la rupture amoureuse au stress post-traumatique. June 20th, 2017. Article.
- Leblanc, J., journaliste. Québec Science (Canada). 85ième Congrès ACFAS (McGill). Réparer les cœurs brisés. May 10th, 2017. Article.
- Perrin, C., journaliste. Médium Large, Radio-Canada Première (Canada). Des pilules pour traiter la peine d'amour. February 15th, 2017. Radio interview available as Webcast.
- Mercure, P., journaliste. La Presse+ (Canada).). Chagrin d'amour ne dure pas toujours. February 14th, 2017. Article.
- Pigeon, S. The McGill Daily (Canada). Rethinking our memories: new trial aims to mitigate pain and suffering. October 3rd, 2016. Article.
- Rand, A., journalist. CJAD (Canada). The Aaron Rand Show. Carrie Fisher, Kevin O'Leary, the heartbreak pill & more. July 18th, 2016. Radio interview available as webcast.
- Nerenberg, A., journalist. The Montreal Gazette (Canada). Montreal research: Broken heart? There might be a pill for you. July 17th, 2016. Article.
- Gang, K. The Concordian (Canada) Migraine medication may cure your heartache. March 29th, 2016. Article.