The Role of Prediction Error in A Behavioral Memory
Reconsolidation intervention For The Treatment of Posttraumatic Stress Symptoms: Original Proposal and Update Due to The Covid-19 Global Pandemic

Benjamin Darnell
bcdarn5547@gmail.com

Follow this and additional works at: https://huskiecommons.lib.niu.edu/allgraduate-thesesdissertations

Recommended Citation
https://huskiecommons.lib.niu.edu/allgraduate-thesesdissertations/6960

This Dissertation/Thesis is brought to you for free and open access by the Graduate Research & Artistry at Huskie Commons. It has been accepted for inclusion in Graduate Research Theses & Dissertations by an authorized administrator of Huskie Commons. For more information, please contact jschumacher@niu.edu.
THE ROLE OF PREDICTION ERROR IN A BEHAVIORAL MEMORY RECONSOLIDATION INTERVENTION FOR THE TREATMENT OF POSTTRAUMATIC STRESS SYMPTOMS: ORIGINAL PROPOSAL AND UPDATE DUE TO THE COVID-19 GLOBAL PANDEMIC

Benjamin Darnell, Ph. D.
Department of Psychology
Northern Illinois University, 2021
David P. Valetiner, Director

A failure to naturally resolve posttraumatic stress symptoms (PTSS) following exposure to a traumatic event is associated with costly and debilitating consequences. Interventions for PTSS are successful for only 40%-70% of patients, and treatment drop-out and symptom relapse are common. Recent research targeting memory reconsolidation mechanisms to augment the memory may provide important information regarding possible paradigms for improving the efficacy of trauma-focused interventions. This research indicates that the use of prediction error during a memory activation cue may result in memory destabilization allowing for the destabilized memory to be updated. Considering that PTSS are inherently memory dependent, an intervention targeting memory reconsolidation mechanisms may be especially relevant for the treatment of these symptoms. The current study was designed to translate the memory reconsolidation literature for clinical application in the treatment of PTSS. Participants were assigned to either the Intervention or the Control conditions. Psychophysiological arousal, as well as change in overall symptoms, intrusion symptoms specifically, and subjective distress were assessed one week later. Although
initially designed as a randomized trial of a behavioral intervention targeting memory reconsolidation mechanism, the onset of the COVID-19 pandemic prevented the completion of planned data collection, and the study was discontinued with only five participants’ data collected in full. Three participants were in the Intervention condition; two were in the Control condition. As such, this data was examined as a case series to explore the potential efficacy of the paradigm. Results of the case series were mixed, suggesting that the Intervention condition, but not the Control condition, may have been successful at diminishing the spontaneous recovery of psychophysiological responding for some individuals ($n = 2$) but that the effect is likely not clinically meaningful. The role of case series in treatment design is discussed, as are limitations of the current design and future directions. A proposal for a future iteration of this study is presented.
THE ROLE OF PREDICTION ERROR IN A BEHAVIORAL MEMORY RECONSOLIDATION INTERVENTION FOR THE TREATMENT OF POSTTRAUMATIC STRESS SYMPTOMS: ORIGINAL PROPOSAL AND UPDATE DUE TO THE COVID-19 GLOBAL PANDEMIC

BY
BENJAMIN DARNELL
© 2021 Benjamin Darnell

A DISSERTATION SUBMITTED TO THE GRADUATE SCHOOL IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE DOCTOR OF PHILOSOPHY

DEPARTMENT OF PSYCHOLOGY

Doctoral Director:
David P. Valentiner
ACKNOWLEDGEMENTS

There are many people without whom this dissertation would not be possible. I would like to thank my committee for letting me attempt a project that was perhaps a bit overly ambitious, not once, but twice, and for being understanding and flexible when the year 2020 was what it was. Thank you to everyone who participated in both iterations of this project for all of your time and effort in what I know were stressful studies; your participation in research like this is what makes progress possible.

I would also like to thank my lab mate, Andrea, for all of her help with both iterations of this project when I know she had much better things to be doing. Thank you to Anna, another lab mate, for her help with the first iteration of this project that, although unsuccessful, was very important in making this dissertation slightly less unsuccessful. Thank you to the lab as a whole for your support in overcoming both individual and common barriers. I would also like to thank my research assistant, Justine, who helped get this dissertation up and running.

Thank you to all my friends who allowed me to hate this project, love this project, and constantly insist that all of their memories are lies. Thank you to my family for their constant support and attempts at understanding, all with a complete lack of reinforcement from me. To my fiancée, Robyn: your love and insistence that this work is a good idea was often the only thing that motivated me to continue; so much of my work in graduate school was only possible because of you and is, therefore, your fault. And last, thank you to anyone who ever
reads this document. I have complete confidence that will only ever be my resilient editor, Susan. Thanks all.
“Remember”

Yet if you should forget me for a while
And afterwards remember, do not grieve:
For if the darkness and corruption leave
A vestige of the thoughts that once I had,
Better by far you should forget and smile
Than that you should remember and be sad.

Christina Rossetti (n.d.)
# TABLE OF CONTENTS

| LIST OF TABLES ...................................................................................................................... xii |
| LIST OF FIGURES ................................................................................................................... xiii |
| LIST OF APPENDICES ............................................................................................................... xv |

Chapter

1. INTRODUCTION AND REVIEW OF LITERATURE ......................................................... 1

   Posttraumatic Stress Symptoms ................................................................. 3

      Significance ............................................................................................................ 3

   Epidemiology and Risk .......................................................................................... 3

   Symptomatology .................................................................................................... 5

   Pathology ............................................................................................................... 7

   Treatment ............................................................................................................. 11

      Therapy as Extinction .................................................................................... 12

   Memory Processes .............................................................................................. 14

      Encoding .............................................................................................................. 14

      Consolidation .................................................................................................... 15

      Reconsolidation .................................................................................................. 18

      Alternative Theories .......................................................................................... 20

   Pharmacological Blockade of Memory Reconsolidation ....................................... 23
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal Models</td>
<td>23</td>
</tr>
<tr>
<td>Human Models</td>
<td>27</td>
</tr>
<tr>
<td>Soeter and Kindt, 2015</td>
<td>27</td>
</tr>
<tr>
<td>Brunet et al., 2008</td>
<td>27</td>
</tr>
<tr>
<td>Brunet et al., 2018</td>
<td>29</td>
</tr>
<tr>
<td>Wood et al., 2015</td>
<td>30</td>
</tr>
<tr>
<td>Behavioral Interference of Memory Reconsolidation</td>
<td>31</td>
</tr>
<tr>
<td>Erasure vs. Extinction</td>
<td>31</td>
</tr>
<tr>
<td>The Retrieval-Extinction Paradigm</td>
<td>33</td>
</tr>
<tr>
<td>Animal Models</td>
<td>33</td>
</tr>
<tr>
<td>Human Models</td>
<td>35</td>
</tr>
<tr>
<td>Schiller et al., 2010</td>
<td>35</td>
</tr>
<tr>
<td>Oyarzún et al., 2012</td>
<td>36</td>
</tr>
<tr>
<td>Björkstrand et al., 2015</td>
<td>37</td>
</tr>
<tr>
<td>Hu et al., 2018</td>
<td>37</td>
</tr>
<tr>
<td>Soeter and Kindt, 2011</td>
<td>38</td>
</tr>
<tr>
<td>Clinical Applications</td>
<td>40</td>
</tr>
<tr>
<td>Maples-Keller et al., 2017</td>
<td>40</td>
</tr>
<tr>
<td>Siegesleitner et al., 2019</td>
<td>41</td>
</tr>
<tr>
<td>Reconsolidation of Traumatic Memories Protocol for the Treatment of PTSD</td>
<td>42</td>
</tr>
<tr>
<td>Visuospatial Interference</td>
<td>44</td>
</tr>
<tr>
<td>Chapter</td>
<td>Page</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>James et al., 2015</td>
<td>45</td>
</tr>
<tr>
<td>Clinical Applications</td>
<td>47</td>
</tr>
<tr>
<td>Iyadurai et al., 2018</td>
<td>47</td>
</tr>
<tr>
<td>Kessler et al., 2018</td>
<td>48</td>
</tr>
<tr>
<td>Ecological Validity</td>
<td>48</td>
</tr>
<tr>
<td>Weems et al., 2014</td>
<td>49</td>
</tr>
<tr>
<td>Kredlow and Otto, 2015</td>
<td>50</td>
</tr>
<tr>
<td>Boundaries of Reconsolidation</td>
<td>51</td>
</tr>
<tr>
<td>Novelty</td>
<td>53</td>
</tr>
<tr>
<td>Prediction Error</td>
<td>55</td>
</tr>
<tr>
<td>Reconsolidation Interference as a Potential PTSS Treatment</td>
<td>57</td>
</tr>
<tr>
<td>The Present Study</td>
<td>60</td>
</tr>
<tr>
<td>Hypotheses</td>
<td>60</td>
</tr>
<tr>
<td>2. METHOD</td>
<td>62</td>
</tr>
<tr>
<td>Participants</td>
<td>62</td>
</tr>
<tr>
<td>Risk, Consent, and Confidentiality</td>
<td>63</td>
</tr>
<tr>
<td>Measures</td>
<td>64</td>
</tr>
<tr>
<td>Outcome Measures</td>
<td>64</td>
</tr>
<tr>
<td>Posttraumatic Stress Symptoms</td>
<td>64</td>
</tr>
<tr>
<td>Sleep</td>
<td>65</td>
</tr>
<tr>
<td>Psychophysiological Arousal</td>
<td>65</td>
</tr>
<tr>
<td>Sleep Conductance Response</td>
<td>66</td>
</tr>
</tbody>
</table>
5. OVERVIEW OF RESULTS AND INTERPRETATION OF PRELIMINARY ANALYSES .............................................................. 91

Control 1 ........................................................................................................................................................................... 91

Overview of Control 1 Results ................................................................................................................................. 91

Average Heart Rate .................................................................................................................................................. 91

Highest Skin Conductance ........................................................................................................................................ 93

Subjective Distress .................................................................................................................................................... 95

Posttraumatic Stress Symptoms ................................................................................................................................ 95

Interpretation of Control 1 Preliminary Analyses ............................................................................................... 97

Control 2 ........................................................................................................................................................................ 98

Overview of Control 2 Results ................................................................................................................................ 98

Average Heart Rate .................................................................................................................................................. 98

Highest Skin Conductance ........................................................................................................................................ 100

Subjective Distress .................................................................................................................................................... 102

Posttraumatic Symptoms ........................................................................................................................................... 103

Interpretation of Control 2 Preliminary Analyses ............................................................................................... 105

Intervention 1 .............................................................................................................................................................. 106

Overview of Intervention 1 Results .......................................................................................................................... 106

Average Heart Rate .................................................................................................................................................. 106

Highest Skin Conductance ........................................................................................................................................ 107
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective Distress</td>
<td>111</td>
</tr>
<tr>
<td>Posttraumatic Symptoms</td>
<td>112</td>
</tr>
<tr>
<td>Interpretation of Intervention 1 Preliminary Analyses</td>
<td>112</td>
</tr>
<tr>
<td>Intervention 2</td>
<td>114</td>
</tr>
<tr>
<td>Overview of Intervention 2 Results</td>
<td>114</td>
</tr>
<tr>
<td>Average Heart Rate</td>
<td>114</td>
</tr>
<tr>
<td>Highest Skin Conductance</td>
<td>115</td>
</tr>
<tr>
<td>Subjective Distress</td>
<td>117</td>
</tr>
<tr>
<td>Posttraumatic Symptoms</td>
<td>120</td>
</tr>
<tr>
<td>Interpretation of Intervention 2 Preliminary Analyses</td>
<td>121</td>
</tr>
<tr>
<td>Intervention 3</td>
<td>123</td>
</tr>
<tr>
<td>Overview of Intervention 3 Results</td>
<td>123</td>
</tr>
<tr>
<td>Average Heart Rate</td>
<td>123</td>
</tr>
<tr>
<td>Highest Skin Conductance</td>
<td>125</td>
</tr>
<tr>
<td>Subjective Distress</td>
<td>126</td>
</tr>
<tr>
<td>Posttraumatic Symptoms</td>
<td>128</td>
</tr>
<tr>
<td>Interpretation of Intervention 3 Preliminary Analyses</td>
<td>129</td>
</tr>
<tr>
<td>Blampied (2011) Technique</td>
<td>131</td>
</tr>
<tr>
<td>Subjective Distress</td>
<td>131</td>
</tr>
<tr>
<td>PTSS</td>
<td>131</td>
</tr>
<tr>
<td>Intrusions</td>
<td>133</td>
</tr>
<tr>
<td>6. DISCUSSION</td>
<td>135</td>
</tr>
<tr>
<td>Chapter</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>The Current Study</td>
<td>136</td>
</tr>
<tr>
<td>Preliminary Analyses</td>
<td>138</td>
</tr>
<tr>
<td>H1</td>
<td>141</td>
</tr>
<tr>
<td>H2</td>
<td>143</td>
</tr>
<tr>
<td>H3</td>
<td>145</td>
</tr>
<tr>
<td>H4</td>
<td>147</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>148</td>
</tr>
<tr>
<td>Skin Conductance</td>
<td>152</td>
</tr>
<tr>
<td>Summary</td>
<td>153</td>
</tr>
<tr>
<td>Conclusions</td>
<td>155</td>
</tr>
<tr>
<td>Considerations Due to the COVID-19 Pandemic</td>
<td>157</td>
</tr>
<tr>
<td>Single-Case Designs for the Development of Novel Interventions</td>
<td>158</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>162</td>
</tr>
<tr>
<td>APPENDICES</td>
<td>185</td>
</tr>
</tbody>
</table>
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Analyses as Originally Proposed</td>
<td>76</td>
</tr>
<tr>
<td>2. Case Series Nomenclature and Associated Descriptions by Phase</td>
<td>82</td>
</tr>
<tr>
<td>3. Results of Case Series Analyses</td>
<td>137</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Flow Chart of the Procedure Process</td>
<td>73</td>
</tr>
<tr>
<td>2. Control 1 Average Heart Rate</td>
<td>92</td>
</tr>
<tr>
<td>3. Control 1 Highest Skin Conductance</td>
<td>94</td>
</tr>
<tr>
<td>4. Control 1 Subjective Distress</td>
<td>96</td>
</tr>
<tr>
<td>5. Control 1 Total PTSS and Intrusion Symptoms</td>
<td>96</td>
</tr>
<tr>
<td>6. Control 2 Average Heart Rate</td>
<td>100</td>
</tr>
<tr>
<td>7. Control 2 Highest Skin Conductance</td>
<td>102</td>
</tr>
<tr>
<td>8. Control 2 Subjective Distress</td>
<td>104</td>
</tr>
<tr>
<td>9. Control 2 Total PTSS and Intrusion Symptoms</td>
<td>104</td>
</tr>
<tr>
<td>10. Intervention 1 Average Heart Rate</td>
<td>108</td>
</tr>
<tr>
<td>11. Intervention 1 Highest Skin Conductance</td>
<td>110</td>
</tr>
<tr>
<td>12. Intervention 1 Subjective Distress</td>
<td>111</td>
</tr>
<tr>
<td>13. Intervention 1 Total PTSS and Intrusion Symptoms</td>
<td>112</td>
</tr>
<tr>
<td>14. Intervention 2 Average Heart Rate</td>
<td>116</td>
</tr>
<tr>
<td>15. Intervention 2 Highest Skin Conductance</td>
<td>118</td>
</tr>
<tr>
<td>16. Intervention 2 Subjective Distress</td>
<td>120</td>
</tr>
<tr>
<td>17. Intervention 2 Total PTSS and Intrusion Symptoms</td>
<td>121</td>
</tr>
<tr>
<td>18. Intervention 3 Average Heart Rate</td>
<td>124</td>
</tr>
<tr>
<td>Figure</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>19. Intervention 3 Highest Skin Conductance</td>
<td>127</td>
</tr>
<tr>
<td>20. Intervention 3 Subjective Distress</td>
<td>128</td>
</tr>
<tr>
<td>21. Intervention 2 Total PTSS and Intrusion Symptoms</td>
<td>129</td>
</tr>
<tr>
<td>22. All Participants Subjective Distress Pre- to Postintervention</td>
<td>132</td>
</tr>
<tr>
<td>23. All Participants PTSS Pre- to Postintervention</td>
<td>133</td>
</tr>
<tr>
<td>24. All participants intrusions pre- to postintervention</td>
<td>134</td>
</tr>
</tbody>
</table>
## LIST OF APPENDICES

<table>
<thead>
<tr>
<th>Appendix</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. FULL DESCRIPTION OF ORIGINALLY PROPOSED ANALYSES</td>
<td>185</td>
</tr>
<tr>
<td>B. FULL CASE SERIES RESULTS</td>
<td>197</td>
</tr>
<tr>
<td>C. PROPOSED THIRD ITERATION OF A BEHAVIORAL MEMORY RECONSOLIDATION FOR THE TREATMENT OF POSTTRAUMATIC STRESS SYMPTOMS</td>
<td>245</td>
</tr>
</tbody>
</table>
CHAPTER 1
INTRODUCTION AND REVIEW OF LITERATURE

Posttraumatic stress symptoms (PTSS) are common following exposure to a traumatic event (Kessler et al., 2005; Spoont et al., 2013). For many, these symptoms naturally resolve (Orcutt et al., 2014); however, for others, symptoms persist with costly and debilitating consequences (Bass & Golding, 2012; Zatzick et al., 1997). Although effective treatments have been designed for PTSS, these treatments are distressing, time consuming, not universally successful, and drop out and relapse are common (Davidson et al., 2001; Ursano et al., 2004). Why some people recover from PTSS and others do not is not fully understood, and many theories have been generated in an attempt to elucidate trauma-relevant processes (e.g., dual representation theory; Brewin et al., 1996; information processing theory; Foa et al., 1989).

Despite many conceptual differences between these theories, one component is generally agreed upon: PTSS are a memory-based condition. Understanding PTSS as memory-based opens avenues of research that may provide an understanding of how PTSS develops and is maintained. Perhaps most importantly, memory research may also offer essential information that could improve the utility and effectiveness of treatment.

One promising avenue of research comes from the literature on basic memory processes. Generally, models of memory suggest that information from the environment is first translated into electrochemical signals (i.e., encoded; Reber, 2013), then stabilized into long-term storage (i.e., consolidated; Nadel & Moscovitch, 1997). Later, this information can be retrieved for use
in working memory. One model, reconsolidation theory, states that when this retrieval occurs under the right conditions, the memory may become unstable and must undergo a process similar to but distinct from consolidation to be stabilized back into long-term memory (LTM; Nader et al., 2000). Termed reconsolidation, if this process is interrupted, the information from the previously consolidated memory may be changed or lost (Nader et al., 2000). The ability to change or erase memories has important implications for the treatment of memory-based conditions like PTSS. Unfortunately, efforts to translate reconsolidation research to clinical use have been met with mixed success. These mixed findings could be attributed to the many parameters (i.e., boundary conditions) that must be met in order for retrieval to result in reconsolidation (Monfils & Holmes, 2018). The current study attempts to design and validate a behavioral protocol within these parameters to target memory reconsolidation interference as a treatment for PTSS.

To provide a rationale for this work, first the significance of PTSS, as well as the epidemiology, symptomatology, pathology, and current treatments, will be discussed. Memory encoding, consolidation, and reconsolidation processes will then be outlined. The current literature on the pharmacological blockade and then the behavioral intervention of memory reconsolidation will be presented. Then, the boundary conditions under which reconsolidation processes may or may not occur will be examined. Finally, the potential for memory reconsolidation interference to be used as a PTSS treatment will be discussed and the present study described.
Posttraumatic Stress Symptoms

Significance

Exposure to a traumatic event and the development of symptoms are quite common. Many, if not most, people in the United States will experience a traumatic event in their lifetimes, and this experience will usually result in PTSS development (Kessler et al., 2005; Spoont et al., 2013). Normally, these symptoms subside naturally; however, 8%-12% of people will fail to recover (Breslav et al., 1991; Breslav et al., 2000; Kilpatrick et al., 2013; Resnick et al., 1993; Roberts et al., 2011). This failure of symptoms to naturally resolve is debilitating and costly. These symptoms may lead to significant functional impairment and low quality of life and may contribute to physical and mental health concerns such as cardiorespiratory problems, gastrointestinal problems, substance abuse, depression, and increased suicide potential (Kilpatrick et al., 2003; Pacella et al., 2013; Panagioti et al., 2009; Zatzick et al., 1997). Treatment is often difficult and time consuming, and may not be effective for all (Davidson et al., 2001; Foa et al., 2009; Ursano et al., 2004). For the individual, these treatments may cost thousands of dollars per year (Bass & Golding, 2012). Nationally, disability compensation for posttraumatic stress disorder (PTSD) costs billions of dollars annually (Bass & Golding, 2012). Clearly, PTSS are a devastating condition for many reasons, and a treatment that is more effective, less time consuming, and less costly is needed.

Epidemiology and Risk

PTSD is the prolonged experience of symptoms (i.e., PTSS) as a result of exposure to a traumatic event. A traumatic event can be any event in which a person is exposed to serious harm...
such as sexual violence, severe injury, or threatened or actual death (American Psychiatric Association, 2013). This exposure can be defined as the direct experiencing or witnessing of the event, hearing of a close friend or family member experiencing the event, or repeatedly being exposed to details of the event as part of one’s job (American Psychiatric Association, 2013). Considering the wide range of events and varying degrees of exposure that can result in PTSD, there can be a great deal of heterogeneity between the traumatic experiences of people who develop symptoms of the disorder.

The prevalence rate for developing PTSD is relatively low among people who experience traumatic events. Although the rates of experiencing such an event range from 39.1% to 89.7% depending on the population, lifetime prevalence rates of PTSD are only 8.3% to 12.3% (Breslau et al., 1991; Breslau et al., 2000; Kilpatrick et al., 2013; Resnick et al., 1993; Roberts et al., 2011). These statistics indicate that simply being exposed to a traumatic event does not guarantee the development of PTSD. There are many factors that have been found to be associated with an increased risk of PTSD development following trauma exposure. Studies have determined that the strongest predictive factors for the development of the disorder are exposure to severe and violent trauma, previous low self-esteem, being in close proximity to the traumatic event, and having a previous mental health diagnosis (Darvez-Borno et al., 1998; Neria et al., 2007). Specific mental health diagnoses that are risk factors for PTSD and that commonly co-occur with the disorder are major depression, anxiety disorders, and substance abuse (Nemeroff et al., 2006). Other potential risk factors may include being female, having a lower level of education, having less social support, and having a large number of other life stressors present at the time (Brewin et al., 2000).
Symptomatology

Considering the heterogeneity of experiences that can result in PTSD, it is not surprising that the disorder can manifest in a wide variety of symptoms. These symptoms are classified by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) into four clusters (Criterion B-E; American Psychiatric Association, 2013) and must be present for at least one month to be considered a PTSD diagnosis (Criterion F; American Psychiatric Association, 2013). Criterion B, intrusions symptoms, are symptoms caused by the traumatic memory being activated or re-experienced in some way that is unwanted and distressing. This cluster of symptoms can include dissociation, distressing dreams, involuntary remembering, and psychological or physiological reactions to cues associated with the memory. Criterion C, avoidance symptoms, manifest as an attempt to avoid trauma-related thoughts, memories, emotions, or physical stimuli (e.g., people, places, things). Negative alterations of mood and cognition, Criterion D, includes loss of memory regarding aspects of the traumatic event, overly negative beliefs about oneself or others, self-blame, incessant negative affect, anhedonia, detachment, and inability to experience positive affect. Criterion E includes alterations in a person’s state of arousal, such as irritability, recklessness, hypervigilance, inability to concentrate, problems sleeping, and having an exaggerated startle response (American Psychiatric Association, 2013). These criteria can manifest in a variety of combinations and degrees of severity, thus PTSS can manifest quite differently from individual to individual.

Although the DSM-5 classifies PTSD as a diagnostic category, research suggests that these symptoms are best viewed as a continuum (Rosen et al., 2008; Spitzer et al., 2007). Studies have shown little evidence of PTSD as a natural class, in which people diagnosed with the
disorder are qualitatively different than people with similar symptoms that do not meet DSM-5 diagnostic requirements (Broome, 2006; Ruscio et al., 2002). In fact, symptoms are often the same regardless of whether the environmental cause was life stress or a traumatic event (Gold et al., 2005), and both PTSD and subclinical PTSS lead to similar functional impairments and low quality of life (Bodkin et al., 2007). These similarities suggest that the distinction between trauma and stress is not necessary to understand PTSS (Gold et al., 2005). Furthermore, comorbidities associated with PTSD are the same for subclinical PTSS; both populations have high rates of anxiety and depression, and both show an increased risk for generalized anxiety disorder and suicidality (Davidson & Smith, 1990; Jackson et al., 2007; Kazak et al., 2004; Lai et al., 2004). Treatment is also the same across populations, with the primary focus being the processing of memories surrounding the stressful or traumatic event (Ehlers & Clark, 2000; Foa & Rothbaum, 1998; Pennebaker, 1997). Considering that symptoms, outcomes, comorbidity and treatment are the same for both PTSD and subclinical PTSS, and considering that there is little scientific evidence to support PTSD as a category, it may be best to conceptualize PTSS as a continuum of symptoms and not a categorical disorder.

Following a traumatic experience, the development of some PTSS is a normal reaction, although the severity, duration, and response pattern of the symptoms may vary (Morina et al., 2014; Orcutt et al., 2014). Once the initial onset of PTSS has occurred, the natural course of those symptoms may follow one of four prototypical response patterns. The most common response to trauma exposure is called resilience (65% as reported by Orcutt et al., 2014), in which there may be a short period of mild PTSS immediately following the traumatic event, followed by a quick and spontaneous return to pretrauma levels of functioning (Bonanno & Mancini, 2012; Morina et al., 2014). The second response pattern, gradual recovery (25% as
reported by Orcutt et al., 2014), is the initial onset of moderate to severe symptoms that gradually reduce back to pretrauma levels over the course of months or years following the trauma exposure (Bonanno, 2005). A small number of individuals will experience the third response pattern, called delayed response (<1%, as reported by Orcutt et al., 2014), with mild to moderate symptoms that become more severe over time (Bonanno & Mancini, 2012), or they may develop the fourth pattern, chronic disruption (2% as reported by Orcutt et al., 2014), in which symptoms are severe for an extended period after the initial trauma (Bonanno, 2005). Orcutt et al. (2014) also reported a “moderate impact – moderate symptoms” pattern (8%), in which people with moderate PTSS pretrauma display high PTSS after the trauma that returns to a moderate level, months later. These many different symptom response patterns and levels of severity that may occur following trauma, coupled with the fact that the onset of some degree of PTSS following trauma is normal, ultimately support the conceptualization of posttraumatic stress reactions as a continuum of symptoms where disorder is characterized by a failure of symptoms to subside.

Pathology

Neurological models outline the biological processes that may underlie PTSS. In these models, the amygdala is responsible for detecting threat and initiating the fight-flight-freeze response (Bisson, 2009). Regions of the brain such as the hippocampus, medial prefrontal cortex (mPFC), and the anterior cingulate cortex (ACC) may all be involved in moderating the amygdala’s response (Bisson, 2009; Layton & Krikorian, 2002). The relationship between these neural regions may be bidirectional, such that amygdala activation may moderate hippocampal, mPFC, and ACC functioning as well (Layton & Krikorian, 2002). This bidirectional relationship
between neural regions suggests that overactivation of the amygdala may result in impaired processing in the hippocampus, mPFC, and ACC, and underactivation in those three regions may lead to overactivation of the amygdala (Bisson, 2009; Layton & Krikorian, 2002). The ultimate result is that emotional content becomes overconsolidated by the amygdala, where declarative content is underconsolidated and disorganized due to impaired hippocampal, mPFC, and ACC functioning (Bisson, 2009; Layton & Krikorian, 2002). This theory explains why people with PTSS present symptoms even when not having conscious recall of the event. It also explains why they often experience intensified memory for the core traumatic event but considerably impaired memory for all other events and details surrounding the trauma.

Several cognitive-behavioral models have been created to explain PTSS onset and maintenance. One such model is dual representation theory (Brewin et al., 1996; Brewin et al., 2010). According to this model, memory consolidation occurs via two related but distinct processes: verbally-accessible memory (VAM) and situationally-accessible memory (SAM; Brewin et al., 2010). The VAM system allows for consolidation and retrieval of conscious experience and contextual memory, including visuo-spatial and temporal information. This system allows for both automatic and deliberate retrieval of this information, as well as the manipulation of this information. According to dual representation theory, the VAM is hypothesized to involve medial-temporal neuroanatomical structures (e.g., the hippocampus) and is connected to cortical structures (e.g., the mPFC).

The SAM system allows for consolidation and retrieval of nonconscious information, including sensory and perceptual information. Importantly, this information cannot be retrieved deliberately and contains no contextual information; therefore, involuntary retrieval of SAM information results in the experience of the information occurring in the present. According to
dual representation theory, the SAM is hypothesized to involve subcortical perceptual structures in the brain. Under normal conditions, information in the SAM system informs memory formation in the VAM system, and information in the VAM system provides contextual information for SAM-based memories. However, dual representation theory also states that, when under extreme stress, amygdala activation results in a diversion of resources to the SAM system, as sensory and perceptual information may be more immediately important for survival than contextual information. The result is overconsolidation of sensory and perceptual information, which is the foundation for PTSS; trauma-related sensory and perceptual information may involuntarily become active, and without ties to contextual VAM memories, the trauma is experienced as happening again in the present. Furthermore, due to the relationship between the SAM system and the amygdala during memory encoding, these intrusive memories trigger an amygdalar response and initiate fight-flight-freeze processes.

For most people, trauma-related SAM information becomes associated with trauma-related VAM information over time. As the SAM information becomes integrated with contextual VAM information, SAM information is no longer experienced as though it is happening in the present. Also, dual representation theory states that connections between the mPFC and the medial-temporal regions of the VAM allow for deliberate control of both VAM and associated SAM information. Thus, PTSS symptoms naturally subside. However, some people avoid posttraumatic SAM information by trying to suppress retrieval and avoid cues. Through this avoidance, SAM information does not have the opportunity to be associated with trauma-relevant VAM information and the PTSS symptoms are maintained.

Dual representation theory and its incorporated neurological model suggest that it is difficulty in the integration of new information into long-term memory (LTM) that results in the
development of the symptoms outlined in the four symptom clusters of the DSM-5: intrusions, avoidance, negative alterations in mood and cognition, and arousal (American Psychiatric Association, 2013). There are many models of the relationships between the symptom clusters and many suggestions as to which cluster is at the core of PTSS (e.g., Brewin et al., 1996; Foa et al., 1995; Horowitz, 1975). One such model describes each cluster by their relationship to intrusion symptoms (Creamer et al., 1992; Steil & Ehlers, 2000). In this model, intrusion symptoms are believed to be central to PTSS, as the other symptom clusters can be explained as ways in which intrusion symptoms are maintained or exacerbated (Creamer et al., 1992; Steil & Ehlers, 2000). Avoidance symptoms are ways of attempting to deal with distressing intrusions by trying to push them away or escape (McFarlane, 1992). Research has shown that avoidance often helps to maintain intrusion symptoms long term (Creamer et al., 1992; Lawrence et al., 1996). It has also been suggested that intrusion symptoms can be exacerbated by the presence of negative alterations in mood and cognitions. Negative thoughts about intrusion symptoms (e.g., “having these uncontrollable memories means there is something wrong with me.”) and distress caused by intrusion symptoms may increase avoidance behaviors, further maintaining the intrusions (Mayou et al., 1993; Rachman & de Silva, 1978; Steil & Ehlers, 2000). Arousal symptoms may increase the severity of all other symptom clusters, which further exacerbates this process of intrusion maintenance (Schell et al., 2004; Tull & Roemer, 2003). Although other formulations of these relationships have been proposed (e.g., Horowitz, 1975), the suggestion of this model that intrusions are at the core of PTSS is in line with dual representation theory; heightened peritraumatic activation of the SAM system generates intrusion symptoms, which when avoided lead to maintained PTSS. Therefore, in accordance with this model of PTSS symptom clusters and dual representation theory, all PTSS symptom clusters may be considered the result of
intrusions and all clusters may work to maintain intrusions; intrusion symptoms can be considered the core symptom cluster of PTSS.

Treatment

There are many treatments available for PTSS. Several prescription drugs, such as selective serotonin reuptake inhibitors, have been shown to be effective pharmacotherapies (Stein et al., 2006). These drugs work by modulating the levels of neurotransmitters that are believed to play a role in acute stress (Stein et al., 2006). Although these drugs have been shown to be better at symptom control than placebos, they merely suppress symptom levels and do not lead to real, lasting change (Lee et al., 2016; Otto et al., 1996; Van Etten & Taylor, 1998). In contrast, psychotherapies have been shown to be equally if not more effective at treating PTSS across all outcome domains (e.g., symptom reduction, patient attrition), while also having long-term efficacy of treatment (Lee, et al., 2016; Merz et al., 2019; Otto et al., 1996; Van Etten & Taylor, 1998).

One meta-analysis has shown both psychotherapy alone and combined psychotherapy and pharmacotherapy lead to greater long-term change in PTSS compared to pharmacotherapy alone (for meta-analytic review, see Merz et al., 2019). No significant differences in treatment efficacy were found between psychotherapy alone and combined psychotherapy and pharmacotherapy (Merz et al., 2019). Furthermore, another meta-analysis found similar results with trauma-focused psychotherapies outperforming pharmacotherapy, combined trauma-focused psychotherapy and pharmacotherapy, and nontrauma-focused psychotherapies (Lee et al., 2016). These meta-analyses suggest psychotherapies, especially trauma-focused psychotherapies, as the front-line treatments for PTSS.
Although these two meta-analyses did not report rates of treatment response, another meta-analysis found that psychotherapies result in 40% to 70% of clients seeing significant reduction in their PTSS (Bradley et al., 2005). This analysis compared exposure-based, cognitive-behavioral, combined exposure and cognitive-behavioral, eye movement desensitization and reprocessing, and other therapies. The total number of participants across all 26 studies was 1,535 and the mean length of treatment was 15.64 hours ($SD = 10.52$). The overall effect size was large for studies that compared PTSS pretreatment to posttreatment ($d = 1.43$), as were the effect sizes when comparing the treatment condition to a wait-list control ($d = 1.11$) or to a control given nontherapeutic support ($d = 0.83$). This pattern of results suggests that psychotherapies are a fairly effective way of treating PTSS. Comparing each therapy to all other therapies included in the study found no major differences in outcome. For all studies combined in the meta-analysis, 56% of participants who entered treatment and 67% of those who completed treatment no longer met DSM criteria for PTSD. Although this meta-analytic finding is impressive considering that PTSS are often a chronic condition, a large portion of the treatment population of each individual study (30% to 60%) did not show significant improvement. This meta-analysis did not look at how long any improvement may have lasted in successfully treated individuals. Considering psychotherapy may be the best available method for PTSS intervention (Lee et al., 2016; Merz et al., 2019), a 30% to 60% rate of nonresponse is disheartening. More research is needed to improve the efficacy of psychotherapies for PTSS.

**Therapy as Extinction**

Exposure-based therapies, specifically prolonged exposure therapy, are some of the most empirically supported treatments for PTSS (Taylor et al., 2003; Foa et al., 2009; Foa et al.,
Generally speaking, the use of exposure therapy is based on the idea that PTSS involves an associative network like those that develop through classical conditioning (McLean & Foa, 2011). In classical conditioning, an unconditioned stimulus (US) provokes an unconditioned response (UR), then is repeatedly paired with another stimulus that is not inherently tied to the UR. Eventually, an association is formed between this second stimulus, called the conditioned stimulus (CS) and the US. This association then leads to an association between the CS and the UR, which continues as a conditioned response (CR) even after the removal of the US.

In the case of PTSS, the US is the traumatic event and the UR is the fear of a negative outcome, such as death or injury (McLean & Foa, 2011). The fear response (the UR) quickly becomes associated with a number of nonthreatening cues (the CS) during the traumatic event, which now trigger the fear (the CR). The associations between the CS and CR are then maintained via avoidance, as avoidance of the CS prevents corrective learning. Exposure therapy works by engaging extinction learning, in which the CS is presented repeatedly without the CR so that corrective learning takes place that does not associate the CS with the CR. For PTSS, the nonthreatening cues are confronted repeatedly with no negative outcome (McLean & Foa, 2011). This confrontation can be done either imaginatively, in which the memories of the traumatic event are recalled in vivid detail, or in vivo. The repeated exposure to these cues (CSs) with no negative outcome (CR) results in the learning that the cues are not associated with the negative outcome, and the fear response diminishes (McLean & Foa, 2011).
Memory Processes

Encoding

Memory encoding is the process of translating raw sensory input data into meaningful information that can be stored in long-term memory (LTM). During any experience, the activation of sensory receptors triggers activation of sensory regions of the brain (Tulving et al., 1994). These regions refine the sensory signals and send them to the appropriate areas for further refinement into a single signal for storage. The areas then ultimately encode the sensory signals into information for storage differ depending on the type of memory that will be created. Implicit memory is the nonconscious memory of procedural tasks and skills, such as how to ride a bike or write your name. These memories are encoded by the areas of the brain involved in motor control, such as the cerebellum, caudate nucleus, and motor cortex (Reber, 2013). Explicit memories can be consciously retrieved and are the memories of events and facts that have been learned. Many regions of the brain may be involved in the encoding of explicit memory with some of the best studied regions within the medial temporal lobe (MTL; Reber, 2013).

The role of the MTL in explicit memory encoding was famously demonstrated by Scoville and Milner (1957) when they removed a large portion of the MTL from patient HM to relieve his epilepsy. After the surgery, HM lost the ability to form new explicit memories, yet was still able to form new implicit memories. This case study demonstrates the differential localization of explicit and implicit memory encoding and highlights the importance of MTL regions for explicit memory formation.
Consolidation

Research since patient HM has demonstrated that MTL regions, specifically the hippocampus, are involved in not just the encoding of explicit memories, but also the consolidation of these memories (Bayley et al., 2003; McClelland et al., 1995; O’Reilly et al., 2014; Squire & Alvarez, 1995; Squire et al., 2001). Memory consolidation is the process following encoding in which the new memory is stabilized and stored into LTM (Nadel & Moscovitch, 1997). This process has been proposed to occur on two levels: through synaptic consolidation, which occurs within hours of memory encoding, and through systems consolidation, which may take days or even years to complete (Dudai, 2004). Synaptic consolidation requires the creation and strengthening of neuronal synapses. For explicit memory, sensory input leads to activation of neurons throughout the cortex and within the hippocampus. The simultaneous firing of the cortex neurons may cause the formation of new synaptic connections between these neurons (Bliss & Gardner-Medwin, 1973; Bliss & Lømo, 1973; Doyère & Laroche, 1992; Hebb, 1949; Konorski, 1948; Morris et al., 1990). These new connections are temporary and may only become stronger and more permanent through continued activation (Kelso et al., 1986; Malinow, 1991; Malinow & Miller, 1986; Sastry et al., 1986). The phenomenon of neurons creating stronger and longer lasting synaptic connections by repeatedly firing simultaneously is called long-term potentiation (LTP; Bliss & Collingridge, 1993). LTP of the cortex neurons may occur due to the activation of the hippocampal neurons. Explicit memory encoding may trigger rapid synaptic formation and activation between hippocampal neurons. It has been theorized that when stimulation of the neurons ends, they perseverate and remain active in what is called a reverberating memory trace (Gerard, 1949;
Hebb, 1949; McGaugh, 1999). The reverberating trace in the hippocampus has been theorized to maintain the memory while facilitating the LTP of the neurons in the cortex (Hebb, 1949; Martinez & Derrik, 1996). The LTP of the neurons in the cortex may strengthen the connections between those neurons, creating permanent structural changes in the cortex, while the reverberating trace in the hippocampus degrades as it becomes less necessary to maintain the memory. It has been proposed that this transfer of activity from the hippocampus to cortical areas may lead to systems consolidation where structural changes in the brain allow the new memories to become independent of the hippocampus (Bontempi et al., 1999; Dudai, 2004; Haist et al., 2001; Wang et al., 2006).

Evidence suggests the presence of emotion during an event as a strong factor that moderates consolidation of an explicit memory (Christianson, 2014). The emotional content of a memory may undergo the memory encoding and consolidation processes in the amygdala (Pelletier et al., 2005). It has been proposed that emotional arousal during an event may shift attention to the source of the arousal and increase alertness, thereby altering the perspective of the event and determining what information gets encoded (Hamann, 2009). This arousal may coincide with amygdala activation, which may under normal circumstances enhance encoding of the episodic content of the explicit memory by upregulating hippocampal activity (Hamann et al., 1999). During highly stressful emotional experiences, however, this relationship may reverse (Bisson, 2009; Layton & Krikorian, 2002). During consolidation of explicit memory, structural changes in the lateral and basal amygdala may result in long-term storage of the emotional content of the memory (Hamann, 2009; Pelletier et al., 2005). The stored emotional content may be connected to other parts of the memory during the consolidation process moderating the
strength and subjective quality of the stored memory (Hamann, 2009; Liang & McGaugh, 1983; Pelletier et al., 2005; Roozendaal & McGaugh, 1996).

The structural changes produced by LTP occurring during consolidation in both the hippocampus and the amygdala may be dependent on a protein synthesis cascade (Nader et al., 2000). This theory suggests that the reverberating memory trace creates an increased rate of depolarization in postsynaptic neurons (Wang et al., 2006). This depolarization may trigger the voltage-gated $N$-methyl-D-aspartate receptor (NMDAR), to increase calcium ion flow into the cell (Bliss & Collingridge, 1993; Tsien et al., 1996). The influx of calcium may activate enzymes that trigger mitogen activated protein kinase (MPAK), which turns on extracellular signal regulated kinase (ERK) through phosphorylation (Tronson & Taylor, 2007). ERK phosphorylates transcription factors such as cyclic AMP-response element binding protein (CREB) and ELK1, which bind to DNA and initiate mRNA transcription. This process may be aided by activation of $\alpha$-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs), which aid in the depolarization of the NMDAR membranes. AMPARs also may increase cyclic adenosine monophosphate (cAMP) which triggers cAMP-dependent protein kinase (PKA), which may directly activate transcription factors or indirectly activate them by phosphorylating ERK and ribosomal protein S6 kinase. The transcribed mRNA upregulates AMPAR, which are important in glucose-dependent intercellular communication. Protein synthesis may also increase the dendritic spine density of the neuron and produce brain-derived neurotrophic factor (BDNF), which is involved in neurogenesis (Rossi et al., 2006; Scharfman et al., 2005). The upregulating of AMPARs and dendritic spine density may increase the postsynaptic neuron's sensitivity to the presynaptic neuron’s signaling, while neurogenesis creates new cells that may wire into the memory formation (Tronson & Taylor, 2007). The result
of this process may be a stabilized neural network that contains a fully consolidated memory (Tronson & Taylor, 2007).

Reconsolidation

For decades, the idea that once memories were consolidated, they were permanently stable and fixed in the brain was the most widely held view of memory processes (Nader, 2013). Recent developments in research have strongly suggested that whenever a memory is retrieved, it becomes labile and requires a process of reconsolidation to be stored in LTM again. This process was first demonstrated by Misanin et al. (1968) using electroconvulsive therapy to block the reconsolidation process; however, reconsolidation did not receive mainstream scientific recognition or support until the publication of a 2000 study by Nader et al. In this study, mice that had been trained to fear a stimulus were given a single exposure to that stimulus one day later in order to activate the fear memory. After activation, the mice received an injection of the protein synthesis inhibiting drug anisomycin directly into the amygdala. Results showed significant impairment to the consolidated fear memory only when the mice had received that single memory activating exposure and only then if the anisomycin injections occurred within six hours of retrieval. This study was the first to show that memories require a protein-dependent reconsolidation process, similar to the initial consolidation process, and that blocking the protein synthesis cascade during reconsolidation impairs a previously consolidated memory (Nader et al., 2000).

The process of reconsolidation involves the same areas of the brain as consolidation, such as the hippocampus and the amygdala (Débiec et al., 2002; Schafe & LeDoux, 2000). However, unlike consolidation, reconsolidation first requires the destabilization of a memory (Alberini &
LeDoux, 2013). It has been suggested that this destabilization is dependent on the degradation of proteins as well as the activation of glutamate receptors, NMDARs, and cannabinoid receptors (Alberini & LeDoux, 2013; Monfils et al., 2009). The reconsolidation of the newly updated memory after destabilization may then require a similar protein syntheses cascade as the one required in consolidation with the activation of NMDARs resulting in morphological synaptic changes and cellular growth (Tronson & Taylor, 2007).

Because of its dependence on protein degradation and synthesis, reconsolidation theory suggests that timing is central to memory reconsolidation (Dębiec et al., 2002; Nader et al., 2000). In this theory, when a memory is retrieved under specific conditions, that memory may become unstable through the process of protein degradation. This degradation process takes time (approximately 3-10 minutes; Monfils et al., 2009). Once the protein degradation has finished, protein synthesis processes are required to reconsolidate the memory back into LTM (Dębiec et al., 2002; Nader et al., 2000). These synthesis processes also take time (approximately 6 hours; e.g., Monfils et al., 2009; Nader et al., 2000). Due to this temporally bound sequence, interference of reconsolidation can only occur at specific times. Interference before or during the degradation process will lead to impaired retrieval or interference of memory destabilization resulting in the memory remaining stable in LTM (e.g., Dębiec et al., 2002; Nader et al., 2000). Only interference during the reconsolidation window, when protein synthesis processes are re-stabilizing the memory, may prevent the memory from being fully reconsolidated into LTM and thus lead to loss of information or memory erasure (Dębiec et al., 2002; Nader et al., 2000).

It is likely that the memory reconsolidation process evolved as a way to efficiently update memories when presented with new and relevant information (Alberini, 2005; Alberini & LeDoux, 2013). An organism with memories that can be updated whenever they are retrieved has
the advantage of being able to learn and form strong memories about danger and rewards without having to re-experience the exact same scenario multiple times (Alberini & LeDoux, 2013). All that is required to update a previously learned memory is a similar or related event to trigger the initial memory, and new information can be integrated and stored. This updating process allows for an adaptively speedy mechanism for learning in a changing environment (Alberini & LeDoux, 2013).

**Alternative Theories**

Although reconsolidation theory has become widely accepted as a mainstream scientific theory of memory interference, other theories attempt to explain the results of memory reconsolidation research through more traditional means (i.e., without suggesting that previously stored memories can become unstable or changed). Two of these theories are memory integration and the temporal context model.

Memory integration attempts to explain the findings from studies purporting to support reconsolidation theory by suggesting that active memories may be malleable but not fragile or able to be fully erased (Gisquet-Verrier & Riccio, 2018). Under this theory, memory is highly state dependent, meaning that the conditions under which the memory is acquired are stored as part of the memory and become necessary for memory retrieval. Therefore, when conditions similar to the initial acquisition occur, the memory becomes active. An active memory is malleable but not able to be fully changed. This malleability is a result of state-dependent learning; when the memory is reactivated, new information from the current environment is associated with the memory structure. These new associations can strengthen the memory by expanding the states under which the memory can be retrieved, or they can weaken the memory
by suppressing associations learned during the initial acquisition. Importantly, it is the newly formed associations that interfere with memory retrieval, not changes to the core memory itself. Furthermore, this theory implies that processes of protein degradation are not required for memory updating; updating is merely a byproduct of changes in state-dependent learning (Gisquet-Verrier & Riccio, 2018). This theory is an interesting alternative to reconsolidation theory and has received some support in studies that have found return of the original memory following established memory erasure paradigms (i.e., reconsolidation interference paradigms; e.g., Duvarci & Nader, 2004; Eisenburg et al., 2003; Gisquet-Verrier et al., 2015). However, memory integration predicts that any state-relevant information presented immediately before, during, or immediately after retrieval may modify the existing memory structure, making this theory less temporally bound than reconsolidation theory (Gisquet-Verrier & Riccio, 2018; Nader et al., 2000). Several studies have demonstrated that information presented before, during, or immediately after memory retrieval does not create lasting change in the memory; only information presented during the reconsolidation window appears to lead to memory augmentation (e.g., Dębiec et al., 2002; Nader et al., 2000; Sinclair & Barense, 2018). For this reason, memory integration does not fully explain the results of all studies that target reconsolidation processes. Differences in the longevity of memory modification following memory reconsolidation paradigms may be better explained by inconsistencies in study methodologies that may determine whether all conditions are met to initiate reconsolidation processes versus new learning via traditional conditioning (e.g., Elsey & Kindt, 2017; Monfils & Holmes, 2018).

Another theory that attempts to counter reconsolidation theory is the temporal context model. According to the temporal context model, memories exist on a two-layer neural network
(see Sederberg et al., 2011). The item layer contains information about the object of the memory and the spatial context in which the memory was acquired. The context layer contains temporal information about the memory including the temporal order of acquired associations in the memory and the temporal context of the memory in relation to other memories. When a memory is retrieved, both layers are activated and new associations with both layers of the old memory are possible. Therefore, the temporal context of the original memory can become associated with the temporal context in which the memory was retrieved. Because of this association, when the memory is later retrieved, both the original temporal context and the retrieval temporal context are activated, leading to source confusion for that memory. The result is a modified memory, where the modification is a result of retroactive interference of the retrieval temporal context on the original temporal context, not actual modification of the original memory trace (Sederberg et al., 2011). Sederburg et al.’s (2011) study supported predictions of the temporal context model; however, the model conflicts with the temporally-bound processes suggested by reconsolidation theory in ways similar to memory integration. Simply put, according to the temporal context model, new information presentation needs to occur temporally close to memory retrieval to create an association of the new information to the old and new temporal contexts now associated with that memory (Sederberg et al., 2011). The result should be that new information presented close to memory retrieval will be more likely to modify later retrieval of the original memory. This hypothesis is directly counter to findings from studies based on reconsolidation theory that demonstrate a necessary delay between memory retrieval and memory interference to allow time for the destabilization of the original memory (Dębiec et al., 2002; Nader et al., 2000). Furthermore, research pitting the temporal context model against reconsolidation theory has shown that a paradigm based on reconsolidation theory (i.e., a delay between retrieval and
interference) is more effective at modifying existing memories than a paradigm based on the
temporal context model (i.e., no delay between retrieval and interference; see Sinclair &
Barense, 2018 for more information on this study).

Pharmacological Blockade of Memory Reconsolidation

Further research has supported memory reconsolidation as a unique process through
selective pharmacological blockade of the protein synthesis cascade. Although the protein
cascade required for reconsolidation is similar to consolidation, animal models have
demonstrated a few key differences. These differences are the activation of the transcription
factor zinc finger 268 instead of BDNF as in consolidation as well as the reversal of the role of
CCAAT-enhancing binding protein-β, which is used exclusively in the amygdala during
reconsolidation but is specific to the hippocampus during consolidation (Alberini, 2005; Tronson
&Taylor, 2007). These differences show that reconsolidation is a unique process, distinct from
both extinction (which involves consolidation mechanisms) and initial memory consolidation.

Animal Models

Animal models of reconsolidation interference have been successful in blocking
reconsolidation of fear memory using pharmacological techniques. When administered
immediately prior or immediately postmemory reactivation, kinase activity inhibitors, protein
synthesis inhibitors, and β-adrenergic or glucocorticoid antagonists have all been shown to be
successful at altering or preventing reconsolidation of the fear memory. A PKA inhibitor
administered directly to the basolateral nuclei of the amygdala resulted in significantly decreased
fear response in rats both one and seven days postinjection (Tronson et al., 2006). Similarly,
injections of the protein-synthesis inhibitors cycloheximide and anisomycin both successfully prevented the return of fear in tests of spontaneous recovery, renewal, and reinstatement 23 days after administration (Duvarci & Nader, 2004; Duvarci et al., 2005). Despite these encouraging findings, translating these results into clinical use is impractical, as many effective pharmacological agents are either toxic to humans or require direct injection into the brain (Monfils et al., 2009). Protein-synthesis inhibitors have also been shown to be significantly less effective when used to block reconsolidation in older memories (Milekic & Alberini, 2002).

Two promising drugs that overcome many of these problems are the β-adrenergic antagonist propranolol and the glucocorticoid antagonist mifepristone. Propranolol has been used to successfully block fear memory reconsolidation in rats, with decreases in fear response being maintained for at least one month (Dębiec & LeDoux, 2004; Przybyslawski et al., 1999). Mifepristone has been shown to similarly block the return of fear in rats 12 days after administration, although these effects were not seen when administered concurrently with propranolol (Pitman et al., 2011). Both drugs are nontoxic to humans and do not require direct injection, making them ideal candidates for the study of reconsolidation interference in humans.

Although propranolol has received considerable attention as a potential agent to target memory reconsolidation processes in humans, one study by Muravieva and Albirini (2010) casts doubt on the efficacy of the drug for all types of fear memories. In this study, the effects of propranolol administration on cued and contextual fear conditioning memories were compared to its effects on a memory of inhibitory avoidance. For the cued and contextual memory, rats were trained to fear a sound in one context (C1). Forty-eight hours later, they were re-exposed to either C1 without the sound (contextual activation) or the sound once in a different context (C2; cued activation) and then received an intraperitoneal (i.p.) injection of propranolol. The rats were
then tested in both C1 and C2 for contextual and cued fear responses respectively. In both cases, no significant difference was found between naïve rats and rats injected with propranolol, suggesting that propranolol blocked reconsolidation of both contextual and cued fear memories following activation.

To test disruption of an inhibitory avoidance memory, rats received a foot shock whenever they entered a dark room in order to train them to avoid that room. Forty-eight hours later, the rats were placed in the dark room and shocked again to activate the memory, receiving i.p. injections of propranolol either immediately before or after testing (T1). Another forty-eight hours later, all rats were tested again (T2) but allowed to avoid the room, in order to assess for inhibitory avoidance. Results showed that the rats who were injected before T1 showed no avoidance during T1, but did show avoidance in T2. Rats injected after T1 showed avoidance during both tests. These results demonstrate that propranolol administered prior to activation did not lead to lasting change in an inhibitory avoidance memory, as indicated by the return of avoidance at T2. Propranolol administered following activation also did not interfere with memory reconsolidation, as indicated by the presence of avoidance at both T1 and T2.

These studies indicate that propranolol blocks reconsolidation of cued and contextual fear conditioning, but does not block the reconsolidation of inhibitory avoidance memories. It may, however, impair retrieval of inhibitory avoidance memories if administered before memory activation as evidenced by the absence of avoidance at T1 but the return of avoidance at T2. These findings suggest that propranolol has limited efficacy when administered for memories involving avoidance. Considering that real traumatic memories involve avoidance, are more complicated, and are often older and stronger than the fear learning memories that are studied in
the lab, this study suggests that pharmacological interventions are not capable of addressing all of the factors that are involved in actual traumatic memories.

An animal study by Ishikawa et al. (2016) has also suggested the NMDA glutamate receptor antagonist and hippocampal neurogenesis promoter Memantine (MEM) as a nontoxic pharmacological intervention for memory reconsolidation disruption. In this study, MEM was administered every day for four weeks following memory acquisition in one sample and memory retrieval in another. MEM was shown to impair retrieval of both the acquired and retrieved memories following those four weeks, presumably through consolidation and reconsolidation interference. However, results of this study suggest that MEM blocks reconsolidation through promoting hippocampal neurogenesis, not through blocking NMDA glutamate receptors (Ishikawa et al., 2016). Hippocampal neurogenesis has been suggested as a potential mechanism for disrupting memory consolidation and reconsolidation, as it may result in remodeling of memory structures that degrades labile memories (Frankland & Josselyn, 2016). In the study by Ishikawa et al. (2016), the reconsolidation interference effects of postretrieval MEM were not significantly different from postretrieval physical exercise (i.e., a behavioral method for promoting hippocampal neurogenesis). Furthermore, MEM was found to be ineffective at targeting amygdala-dependent memories, perhaps due to its hippocampal-neurogenesis-specific mechanism of action. Considering the role of the amygdala in trauma-related memories (Bisson, 2009; Layton & Krikorian, 2002), MEM may not be an effective method for targeting reconsolidation interference to treat PTSS.
Several studies have successfully translated findings from the animal literature on pharmacological blockade of memory reconsolidation to human use (e.g., Kindt et al., 2014). Importantly, a few of these studies have attempted to apply this research to treat clinical and subclinical populations, for both specific phobia and PTSS. One such study used postretrieval propranolol to target subclinical fear of spiders (Soeter & Kindt, 2015). Participants were told that they were going to touch a tarantula, then were led into a room with a tarantula in an open terrarium. After two minutes of exposure, the participants were led out of the room without ever having touched the animal. They were then given 40mg of propranolol. Both one day and one year later, participants were able to approach and touch the tarantula with minimal distress. This binary transition from avoidance to approach of the tarantula was not seen in the placebo control (Soeter & Kindt, 2015). This study is instrumental in demonstrating the clinical utility of reconsolidation-based interventions; however, the memories involved in specific phobias are arguably less complex than those in PTSS, and activation of these memories requires a relatively simple cue.

Only two studies have examined a pharmacological intervention targeting memory reconsolidation of PTSS-related memories. The first is a study by Brunet et al. (2008) that examined the effects of propranolol on memory reconsolidation in individuals with diagnostic PTSD. Nineteen participants wrote in detail about the traumatic event that caused their PTSD
symptoms. This writing involved the preparation of two scripts per participant with each script targeting a different aspect of their traumatic event. When the writing was complete, the researcher read each script and requested more information when necessary. This script preparation procedure activated the trauma memory, after which participants were randomly assigned to receive either 40 mg short-acting propranolol or a placebo.

After a week had passed, participants returned to the lab for the follow-up procedure. Baseline heart rate (HR), skin conductance (SC), and electromyogram (EMG) responses were recorded for 30 seconds. After baseline data was collected, participants listened to 30-second recordings of each of their two scripts. These scripts were composed and prerecorded by the researcher. After listening to these scripts, the participant was asked to imagine the traumatic event for 30 seconds. Responses for HR, SC, and EMG were calculated by subtracting the mean follow-up baseline score from the mean imaginal exposure score. A multivariate analysis of variance (MANOVA) was used to analyze the psychophysiological data with HR, SC and EMG as dependent variables. Psychophysiological responses were also subjected to independent t tests.

Analyses found HR and SC of participants to be significantly lower in the propranolol condition compared to the placebo control. HR and SC were also found to be below the typical PTSD cutoff for the propranolol condition and not for the control, although only HR was significantly lower. EMG was not found to be significantly different between conditions, and both the propranolol and the placebo conditions showed EMG responses below the typical PTSD cutoff. The effect sizes (Cohen’s d) were found to be very large for SC (d=1.23), large for HR (d=0.92), and small for EMG (d=0.29). Despite the poor EMG results, the findings from this
study using HR and SC support the effectiveness of propranolol to block reconsolidation in human subjects.


The study by Brunet et al. (2008) was followed by a 2018 randomized controlled trial using a similar paradigm. In this study, 60 participants with diagnostic PTSD were randomly assigned to be given propranolol one hour prior to memory activation, via writing a one-page trauma narrative (Brunet et al., 2018). This narrative took approximately 30 minutes to write, and was required to be in the present tense, be in the first person, focus on the most disturbing aspects of the trauma, and include five or more bodily sensations from a predetermined list. Following writing the narrative, the participant was asked to read the narrative once out loud to the experimenter. Once weekly for the next six weeks, the participants were given a dose of propranolol, then 90 minutes later were asked whether they needed to add or change any part of their narratives. They were then asked to re-read the narrative once to the experimenter. Results demonstrated that participants PTSD symptoms decreased significantly more in the propranolol condition compared to placebo controls. Pre- to posttreatment effect sizes were $d = 1.64$ and $d = 0.72$, respectively using the clinician-administered PTSD scale (CAPS; Blake et al., 1995), and $d = 2.63$ and $d = 0.51$, respectively using the PTSD checklist – Specific (PCL-S; Weathers et al., 1993). Intent-to-treat effect sizes were $d = 1.76$ and $d = 1.25$, using the CAPS, and $d = 2.74$ and $d = 0.55$, respectively using the PCL-S (Brunet et al., 2018). These results further demonstrate that pharmacological intervention of memory reconsolidation via propranolol may be an effective means for PTSS treatment.
Wood et al. (2015).

Although the studies by Brunet et al. (2008, 2018) suggest that a pharmacological memory reconsolidation intervention may be effective for PTSS, these findings have not been demonstrated in similar studies. Three studies by Wood et al. (2015) examined the reconsolidation interference capabilities of propranolol, mifepristone, and combined mifepristone and D-cycloserine, a NMDA partial agonist that may enhance learning and extinction (Monahan et al., 1989; Richardson et al., 2004). In all three studies, participants with PTSD were asked to describe their traumatic event in order to retrieve the memory and drugs were administered. One week following the activation trial, participants returned and engaged in script-driven traumatic mental imagery while HR, SC, and EMG responses were recorded. None of the three studies found any physiological differences between control and experimental conditions, nor were any decreases in PTSS observed.

This study contradicts the findings of Brunet et al. (2008, 2018) suggesting that pharmacological interventions may have difficulty targeting memory reconsolidation processes in humans. The activation and completion of memory reconsolidation only occurs under certain boundary conditions, and it is likely that these contradictory findings are due to Wood et al. (2015) inadvertently violating one of these boundaries. For example, research has suggested that reconsolidation processes are only activated when novel or contradictory information is presented during activation (Díaz-Mataix et al., 2013; Sevenster et al., 2014; Sevenster et al., 2013; Winters et al., 2009) and when the activation cue is neither too short nor too long, with the duration of the cue being determined by the age and the salience of the memory (Bustos et al., 2009; Frankland et al., 2006; Lee et al., 2006; Robinson & Franklin, 2010). It is possible that the
Brunet et al. (2008) study used more accurate cue durations for their sample than Wood et al. (2015), or that they inadvertently introduced sufficient novel information where Wood et al. (2015) did not. Unfortunately, pharmacological interventions are rigid in their administration and cannot be easily tailored to the complexities of traumatic memories and the boundaries that govern memory reconsolidation. Considering the limited support between Brunet et al., (2008, 2018) and Wood et al. (2015) for the efficacy of drugs for human reconsolidation interference as a treatment for PTSS, as well as the evidence from animal models that pharmacological blockade of reconsolidation may not be possible with avoidance relevant memories, a behavioral intervention to target reconsolidation processes may provide a more flexible and reliable method for human reconsolidation interference.

**Behavioral Interference of Memory Reconsolidation**

**Erasure vs. Extinction**

In studies looking at nonpharmacological methods of reconsolidation interference, most paradigms compare memory erasure to extinction. Reconsolidation interference and extinction differ procedurally, biologically, and cognitively as well as in the outcomes they produce. Reconsolidation is activated by a short memory re-exposure, but a long re-exposure triggers extinction (Eisenburg et al., 2003; Kim & Fanselow, 1992; Pedreira & Maldonado, 2003; Suzuki et al., 2004). This difference has been demonstrated by using protein synthesis inhibitors to target fear memories in mice after both short and long memory re-exposures (Suzuki et al., 2004). After short re-exposure, the memory is attenuated as the inhibition of the protein synthesis cascade results in interference with the memory reconsolidation process. After the long re-
exposure, the memory remains unaffected, as protein inhibition blocks the consolidation of the new extinction memory (Suzuki et al., 2004). These different re-exposure lengths activate different anatomical regions of the brain to initiate their respective processes. Extinction of fear memories seems to occur primarily in the amygdala and mPFC, and reconsolidation processes occur in the amygdala and hippocampus (Burgos-Robles et al., 2007; Dębiec et al., 2002; Mamiya et al., 2009; Santini et al., 2004).

On the cognitive level, these two processes differ in their relationship to the original fear memory. Extinction does not result in the weakening of the stimulus-response association as evidenced by the return of fear phenomena. These phenomena are ways in which the fear association may be detected after successful extinction. Reinstatement occurs when exposure to the US leads to the return of fear when the CS is later presented. Context renewal is when exposure to a new environment following extinction results in the return of fear. Reacquisition is when fear learning occurs significantly faster for a subject with an extinguished fear than for a naïve subject. Spontaneous recovery is when the fear association returns unprovoked as a function of time. The existence of these phenomena suggest that extinction does not lead to the weakening or elimination of a learned fear. Instead, extinction results in the development of a new memory that competes with the fear association (Alberini, 2013). At first, this new memory is able to suppress the effects of the fear memory; however, over time or under certain conditions, the fear memory can override the extinction memory and result in the return of fear.

Demonstration of memory erasure requires the absence of any of the return of fear phenomena; a subject with an erased memory should appear no different than a naïve subject. Since memory reconsolidation interference does not create a new memory but instead disrupts the original memory, it is able to permanently weaken or erase fear associations (Alberini, 2013).
In a paradigm looking at memory erasure versus extinction in a population with PTSS, intrusion symptoms could be used as a proxy for return of fear. Intrusions are necessarily memory dependent, as they often involve the unwanted re-experiencing of the traumatic event (Hackmann et al., 2004; Steil & Ehlers, 2000). In this paradigm, the recovery from and eventual return of intrusions may therefore be considered a marker of extinction where the permanent elimination of these symptoms would mark reconsolidation interference.

The Retrieval-Extinction Paradigm

Animal Models

A paradigm to erase fear memories during the reconsolidation window, called the retrieval-extinction paradigm or postretrieval extinction, has been successfully developed using animal models. This paradigm was developed and tested by Monfils et al. (2009) in a series of six experiments. In the first experiment, the effect of this paradigm on spontaneous recovery was examined. Rats were conditioned to fear a stimulus, then 24 hours later that fear memory was activated. After activation, extinction trials were administered either during the reconsolidation window (10 minutes or one hour after activation) or outside the window (six or 24 hours). One month following activation, rats that received extinction training outside the reconsolidation window, but not the rats that received training inside the window, showed spontaneous recovery of fear as measured by freezing response (Monfils et al., 2009).

The second and third experiments assessed the behavioral paradigm’s effect on context renewal and reinstatement of fear, respectively (Monfils et al., 2009). In the renewal experiment, rats were conditioned to fear a stimulus in context A, then 24 hours later either received an
activation trial in context B followed by extinction or just received extinction. One day later, the rats were tested for the return of fear in context B, then 24 hours following were tested again in context A. This study found that rats that did not receive the activation trial showed renewal of fear in the context in which the fear memory was first formed. Rats that did receive the activation trial did not show fear renewal. In the reinstatement experiment, rats were trained to fear a stimulus by pairing it with a foot shock, then received a series of unpaired shocks 24-hours after memory activation and extinction. The next day, testing for reinstatement of fear revealed that only the mice that received the activation trial did not experience reinstatement (Monfils et al., 2009).

Two other experiments by Monfils et al. (2009) demonstrate that behavioral interference of memory reconsolidation leads to decreased reacquisition of fear by showing that rats have significantly more difficulty being reconditioned to fear a stimulus after completing the behavioral intervention paradigm. These studies used a single pairing and five pairings to recondition the animals, respectively. The final of the six studies demonstrated the differing molecular mechanisms between behavioral interference of memory reconsolidation interference and extinction. All six of these studies together demonstrate the ability of a behavioral intervention to target distinct reconsolidation processes to permanently erase fear (Monfils et al., 2009).

Efforts to replicate and extend the findings of Monfils et al. (2009) for both fear- and non-fear-based memories have resulted in mixed success. Animal studies using the retrieval-extinction paradigm have successfully demonstrated the paradigm’s efficacy at engaging and interfering with reconsolidation; however, the literature is mixed as to whether this interference results in decreased (Chan et al., 2010; Clem & Huganir, 2010; J. Liu, et al., 2014) or increased
fear responding (Stafford et al., 2013), or if interference is possible in all circumstances (Chan et al., 2010; Clem & Huagnir, 2010). The efficacy of this paradigm may be highly dependent on several boundary conditions that influence the initiation of reconsolidation processes and the malleability of memories during the reconsolidation window. Continued research is needed to identify these boundary conditions; however, the animal literature on the retrieval-extinction paradigm is promising, and efforts to translate these findings to human use have been successful.

**Human Models**

Schiller et al. (2010). The retrieval-extinction paradigm was first successfully translated to human use targeting fear-relevant memories by Schiller et al. (2010) for laboratory-conditioned fear. Participants in this study underwent fear conditioning to an electric shock, then one day later were given extinction training either with or without prior memory retrieval. Those that were in the memory retrieval condition were further divided into a condition that received training 10 minutes after retrieval and a condition that received training six hours after retrieval. Spontaneous recovery was assessed 24 hours later by measuring participant SC response when presented with the CS without the US. Reinstatement was assessed both one day and one year later by measuring participant SC response when presented with only the CS after experiencing four unsignaled shocks in the original experiment room. All three conditions showed a significant increase in fear response as measured by SC after conditioning followed by a return to nonsignificant levels of fear following extinction. Both one day and one year after testing, the return of fear was found in the no-retrieval and the retrieval-six-hour conditions, but not the retrieval-10-minute condition, consistent with extinction conducted within a specific time window after memory retrieval permanently eliminating the fear memory.
Oyarzún et al. (2012). The findings of Schiller et al. (2010) were replicated by Oyarzún et al. (2012) using a within-subjects design and auditory aversive stimuli. In this study, all participants underwent conditioning with three differently colored squares as stimuli. Two of these squares were paired with two different aversive sounds, resulting in the conditioned fear of these squares. The third square was used as a neutral stimulus with no sound pairing. One day after conditioning, a single presentation of the neutral stimulus was administered along with a single presentation of one of the fear-conditioned stimuli in order to activate the learned fear memory for that stimulus (Stimulus A). The other fear-conditioned stimulus was not used in a memory activation trial (Stimulus B). Immediately following the memory activation trial for Stimulus A, fear extinction trials were conducted for both Stimulus A and B, and a similar trial was conducted with the neutral stimulus. The following day, spontaneous recovery and reinstatement of fear were tested for both fear conditioned stimuli. Both spontaneous recovery and reinstatement were significantly decreased for Stimulus A compared to Stimulus B as measured by SC. There were no significant differences in spontaneous recovery or reinstatement between Stimulus A and the neutral stimulus. These findings show a return of fear only with the fear-conditioned stimulus that did not receive an activation trial prior to extinction (Stimulus B). In contrast, the fear-conditioned stimulus that did receive the activation trial (Stimulus A) elicited the same amount of fear response as a nonfeared stimulus (the neutral stimulus). These results suggest that this behavioral paradigm successfully erases fear memory, so that a fear-relevant stimulus becomes no different than a neutral stimulus and both are significantly different from a fear-relevant stimulus that was simply extinguished. Because this study was able to replicate the findings of Schiller et al. (2010) using a novel feared stimulus (aversive auditory
stimuli vs. electric shock), this study supports the use of this behavioral paradigm for reconsolidation interference for a variety of stimuli.

Björkstrand et al. (2015). The Schiller et al. (2010) study was further replicated by Björkstrand et al. (2015). Participants in this study were trained to fear a visual stimulus by pairing that stimulus with an electric shock. The next day, participants received a two-minute memory-activation trial, then received extinction training either 10 minutes or six hours later. One day later, renewal of fear was tested with fMRI scans of the basolateral amygdala. Participants who had received extinction training 10 minutes following memory activation demonstrated less basolateral amygdala activity compared to those who received extinction outside the reconsolidation window (six hours after activation). The amygdalar activation of the later condition predicted fear reacquisition in participants tested 18 months after fear conditioning as measured by SC. The results of this study show that the return of a learned fear association at three days and 18 months postconditioning was present in only the condition that received extinction training outside the reconsolidation window (the six-hour condition). These findings also successfully demonstrate the ability of a behavioral paradigm to permanently erase laboratory-conditioned fear memories in humans.

Hu et al. (2018). Further validation of the retrieval-extinction paradigm was conducted by Hu et al. (2018). In this study, 155 human participants completed a three-day protocol. On Day 1, participants were trained to associate a visual stimulus with an electric shock. One day later, participants completed a retrieval-extinction paradigm with the learned fear association from Day 1, with either a 1-second, 4-second, 30-second, or 3-minute retrieval cue. Finally, one day later, the participants were tested for fear recovery and reinstatement. Recovery was tested by SC during presentation of the cue without the paired shock; reinstatement was tested by SC during
administration of several shocks and subsequent presentation of the cue without the paired shock. Results of the study suggest that recovery and reinstatement of fear only occurred for participants whose retrieval cue during the retrieval-extinction paradigm (Day 2) was too long (i.e., 30 seconds, 3 minutes). Participants with Day 2 retrieval cue durations of 1 second or 4 seconds did not demonstrate significant return of fear. These results not only provide further evidence for the utility of the retrieval-extinction paradigm to attenuate fear memories in humans, they also demonstrate consistency with the temporal assumptions of reconsolidation theory. According to reconsolidation theory, timing of the memory retrieval is important; too long of a retrieval will result in engagement of extinction processes and will allow for the return of fear (Suzuki et al., 2004). Hu et al.’s (2018) study provides further support for the retrieval-extinction process by demonstrating this temporal assumption in action, as longer retrieval cue durations predicted return of fear despite successful Day 2 extinction.

Soeter and Kindt (2011). Some human research using the retrieval-extinction paradigm has produced mixed results. A study by Soeter and Kindt (2011) looked at both pharmacological and behavioral intervention of memory reconsolidation in humans. In this study, participants underwent fear learning to two fear-relevant stimuli for both the drug and the behavioral paradigms. On the second day for the drug paradigm, participants received either a single dose of propranolol or a placebo immediately prior to memory activation of one of the stimuli. For the behavioral paradigm, participants engaged in activation of one of the stimuli, then waited 10 minutes before extinction trials were administered for both stimuli. On the third day, participants in the experimental conditions for both the drug and behavioral paradigms showed no spontaneous recovery as measured by fear-potentiated startle response (FPS) compared to the control stimulus. Participants in the pharmacological but not the behavioral paradigm showed no
reacquisition of fear as measured by FPS. No difference was found for SC and subjective units of distress (SUDS) between the experimental and control stimuli for either paradigm.

This study partially conflicts with the findings of previous studies (e.g., Brunet et al., 2008; Schiller et al., 2010), as differential SC activation between experimental and control stimuli was not demonstrated. This discrepancy is particularly troubling, as SC is the most common method of measuring fear response in studies of memory reconsolidation interference (e.g., Björkstrand et al., 2015; Brunet et al., 2008; Oyarzún et al., 2012; Schiller et al., 2010; Wood et al., 2015). Another problematic finding was the limited efficacy of the behavioral paradigm. Although both propranolol and postactivation extinction trials led to decreased spontaneous recovery, only participants in the behavioral paradigm showed fear reacquisition. These problematic findings might be explained by differences between this study and other more successful research. Most importantly, other studies have shown that activation cues need to be longer for stronger memories (Frankland et al., 2006; Robinson & Franklin, 2010). Soeter and Kindt (2010) utilized similar length activation cues as used in previous studies despite their stimuli being more fear-relevant (i.e., pictures of a spider and a gun) compared to the fear-conditioning stimuli in other research (i.e., colored shapes). It is possible that these fear-relevant stimuli are more strongly consolidated in memory and therefore require a longer activation cue. It is also possible that, due to the increased fear-relevancy of the stimuli, participants continued to think about the stimuli during the 10-minute break between activation and extinction in the experimental condition. Failing to cognitively disengage with the stimuli would mean that no real break occurred between the activation trial and extinction, effectively turning the activation trial into the first extinction trial and engaging extinction mechanisms instead of reconsolidation processes (Bustos et al., 2009; Lee et al., 2006). In order to ensure that reconsolidation is
activated over extinction, participants would need to be distracted from the fear-relevant stimuli during the break between activation and extinction. These two limitations of the Soeter and Kindt (2010) study represent two important boundaries that determine whether a memory is successfully destabilized and whether memory reconsolidation interference is possible.

Clinical Applications

Maples-Keller et al. (2017). Despite the mixed findings regarding the utilization of the retrieval-extinction paradigm to target fear-based memories in humans, the success of many of these studies has led researchers to pursue this paradigm as a possible treatment for fear-memory-based disorders. One study used this paradigm to target fear memories of human participants with a specific phobia of flying (Maples-Keller et al., 2017). Participants ($n = 89$) completed eight sessions of treatment. The first session consisted of psychoeducation and treatment planning. Sessions 2 to 4 focused on anxiety management, including cognitive restructuring, breathing retraining, and hyperventilation exposure. Sessions 5 to 8 were the retrieval-extinction sessions. In these sessions, participants received a 15-second retrieval cue, followed by a 10-minute break then virtual reality exposure to an individualized fear hierarchy (e.g., walking through an airport terminal, sitting on an airplane with the engines off). Each participant received one of two cues for the course of their exposures: either a virtual reality video clip of a plane taxiing and taking off with audio or a virtual reality neutral clip of a living room. Follow-up assessments were conducted at posttreatment, 3 months, 6 months, and 12 months using clinical and psychophysiological measures. Psychophysiological follow-up assessments were conducted only at posttreatment and the 3-month follow-up and were conducted in a novel environment to test for context renewal of fear. Results found no significant
differences between the neutral cue condition (i.e., the control condition) and the flying cue condition (i.e., the experimental condition) on any clinical measure. Significant differences were found at posttreatment and 3 months for the HR and SC measures, suggesting that the experimental condition showed improved psychophysiological responding compared to the control condition. Results of this study suggest that the retrieval-extinction paradigm may attenuate fear for people with a specific phobia of flying on the physiological level, but that this change may not be reflected on the conscious level (as measured by clinical self-report measures) when compared to traditional extinction paradigms. This study demonstrates that the retrieval-extinction paradigm can be successfully used to treat clinical fear-based disorders, and that the mechanism of change may be primarily through physiological, as opposed to cognitive, processes (Maples-Keller, et al., 2017).

Siegesleitner et al. (2019). The retrieval-extinction paradigm has also been adapted to target PTSS using a trauma analogue study (Siegesleitner et al., 2019). In this study, 107 female participants were exposed to a video of a violent sexual assault on Day 1. One day later, they were exposed to a retrieval cue of 11 still images from the video, each presented for two seconds and in the same order as they appeared in the film. A 10-minute delay followed, then participants were given one of three interventions: imagery rescripting, imagery rehearsal, or no intervention. For the imagery rescripting condition, participants were asked to vividly recount the violent film but were instructed to change the film in any way that wished to result in a more positive outcome (i.e., to disempower the perpetrator and save the victim). For the imagery rehearsal condition, participants were asked to vividly recount the film but were not asked to change the film in any way. For the no-intervention condition, participants read a neutral magazine for 15 minutes. Follow-up assessments were conducted six days later. Results demonstrated no
significant differences between conditions on the number of intrusion symptoms experienced during the six days prior to the follow-up assessment. However, the imagery rescripting condition was found to be less distressing for participants than the other two conditions, and it resulted in a more rapid decline of intrusions. These results may indicate that imagery rescripting during the retrieval-extinction paradigm may lead to a more rapid recovery from aversive experiences. More research is needed to replicate these findings and determine whether the mechanism of improvement is primarily through changes in physiological arousal (i.e., Maples-Keller et al., 2017). Despite the limitations of using a trauma analog, this study provides some evidence that the retrieval-extinction paradigm may be clinically useful in treating PTSS.

Reconsolidation of traumatic memories protocol for the treatment of PTSD. More research is needed to determine the efficacy of the retrieval-extinction paradigm for treatment of PTSS. However, several treatment protocols have been developed based on research conducted with this paradigm. Notably, proponents of the exposure-based PTSS treatment eye movement desensitization and reprocessing (EMDR) and its derivatives (i.e., motion-assisted multimodal memory desensitization and reprocessing; Jetly et al., 2017) claim that these treatments’ mechanism of action is through reconsolidation processes (Jetly et al., 2017; Shapiro, 2017). However, EMDR was developed as a treatment prior to its ties to reconsolidation theory; thus, these theoretical claims have occurred entirely posthoc. Furthermore, these treatments’ protocols do not parallel the retrieval-extinction paradigm, or any other reconsolidation paradigm from the literature. Therefore, although these treatments may involve reconsolidation processes, these claims have yet to be sufficiently verified and a discussion of EMDR is not necessary for this review.
Similar arguments could be made for the reconsolidation of traumatic memories (RTM) protocol for the treatment of PTSD (Tylee et al., 2017). RTM was developed as a treatment for PTSS prior to its association with memory reconsolidation and its subsequent name change; however, the protocol has since been standardized and explicitly tied to the retrieval-extinction paradigm. In this protocol, people with PTSS are asked to briefly recount their trauma narrative. This narrative is abruptly interrupted once it is observed that the individual is experiencing physiological arousal. Following this interruption, the individual is reoriented to the therapy context. Starting and stopping points of the trauma memory are then identified, and the individual is guided through construction of an imaginary movie theater. The individual is then guided through an imaginary screening of a black-and-white film of their trauma memory from beginning to end repeatedly until they habituate. They repeat this procedure with an imaginary screening of a color film of their trauma memory quickly and in reverse order (i.e., end to beginning) until the habituate. Individuals are asked to imagine several identified triggers of their physiological arousal. Then they are asked to describe several nontraumatizing alternate accounts of their trauma narrative of their own design before finally recounting their original trauma narrative as a whole (Tylee et al., 2017).

RTM is clearly adapted from the retrieval-extinction paradigm as it includes a brief memory retrieval cue, then a delay, followed by exposure. Research on this protocol has suggested that it is more effective than wait-list controls at decreasing PTSS at two-week ($g = 4.20$), six-week ($g = 3.63$), six-month ($g = 3.59$), and 12-month ($g = 6.48$) posttreatment follow-up assessments using a population of male veterans with PTSD (Gray et al., 2017; Tylee et al., 2017). Despite this preliminary success, RTM has yet to be examined in comparison to other active PTSS treatments. RTM includes elements of graduated extinction (e.g., starting the
imaginal exposure with the black-and-white film and later moving to color) and imagery rescripting (e.g., description of alternative, nontraumatizing accounts of the trauma narrative) within the context of the retrieval-extinction paradigm. Research comparing RTM’s efficacy to the efficacy of these and other paradigms in treating PTSS is necessary to determine RTM’s clinical utility above and beyond existing treatments. Furthermore, more research is necessary to determine if the primary mechanism of action is the retrieval-extinction framework of the protocol, as would be expected based on reconsolidation theory. More research is therefore needed to establish the retrieval-extinction paradigm as an effective PTSS intervention and to determine if the full RTM protocol is necessary for effective treatment.

**Visuospatial Interference**

The retrieval-extinction paradigm is not the only paradigm designed to target memory reconsolidation interference for the modification of fear memories. Another behavioral reconsolidation paradigm, here called visuospatial interference, uses visuospatial tasks to disrupt memory reconsolidation of fear memories. Fear memories, such as intrusion symptoms in PTSS, involve mental images containing visual and spatial information (Brewin, 2014). For example, the memory of being assaulted in a park involves visual information such as a statue, greenery, etc., and spatial information such as the position of the statue in relation to the victim’s position, etc. Holding a mental image, including a fear memory, in working memory requires the use of visuospatial working memory (Pearson et al., 2015). Working memory is limited in capacity, so taxing working memory can interfere with information that is currently or was recently held in working memory (Baddeley, 2000, 2012). This model of working memory has important implications for reconsolidation theory; if a memory can be retrieved from LTM into working
memory, taxing working memory while the retrieved memory is unstable may interfere with or prevent reconsolidation of that memory (James et al., 2015). One task that has been used most frequently in the reconsolidation literature to tax working memory, specifically visuospatial working memory, is the computer game Tetris.

Tetris requires spatial manipulation of blocks of different shape and color. Research has demonstrated that the task leads to neural activation of regions of the brain involved in visuomotor processing (e.g., sensory-motor cortical areas, occipitoparietal regions; Price et al., 2013; Rietschel et al., 2012), and that repeated Tetris practice leads to improved performance on other visuospatial tasks (Belchior et al., 2013; Moreau, 2013; Terlecki et al., 2008). Furthermore, one study has demonstrated that cumulative Tetris total scores over a five-minute play period selectively predicts visuospatial working memory performance, but not performance on tasks designed to test other cognitive processes (i.e., verbal reasoning, nonverbal reasoning, verbal short-term memory, visuospatial short-term memory, verbal working memory; Lau-Zhu et al., 2017). Due to its demonstrated specificity to visuospatial working memory, research has started to examine Tetris’s efficacy at interfering with the consolidation and reconsolidation of visuospatial memories like fear memories.

James et al., 2015

The first studies to test the utility of Tetris to modify fear memory were conducted by James et al. (2015) using a trauma analog. In the first study, participants completed a three-day trauma film paradigm. On Day 1, participants played three minutes of Tetris, followed by viewing a 12-minute film involving several traumatic scenes (e.g., a man drowning). They were then sent home and asked to record every intrusive memory of the film they experienced until the
next session. One day later, participants returned to the lab and were assigned to one of two conditions: the retrieval plus Tetris (experimental) condition and the no-retrieval and no-Tetris (control) condition. Participants in the experimental condition watched 11 static images of the film from Day 1, each image two seconds apart. This retrieval task was followed by a 10-minute break, then 12 minutes of Tetris. The control condition only completed the 10-minute break followed by 12 minutes of sitting quietly. Participants were then sent home with the instructions to continue recording every intrusive memory of the film until their final session. One week later, participants returned to the lab with their journal to complete follow-up assessments. Results of this study demonstrated that participants who played Tetris following memory retrieval had fewer intrusive memories of a trauma film compared to the control condition ($d = 1.14$). Furthermore, the frequency of intrusive memories declined significantly faster for participants who played Tetris compared to the control condition.

James et al. (2015) conducted a second study to further test whether postretrieval Tetris gameplay interferes with memory reconsolidation. The procedures for this study were the same as the first but with two additional conditions. The four conditions were: retrieval plus Tetris, no retrieval and no Tetris, Tetris alone, and retrieval alone. Results of this second study demonstrated that the retrieval plus Tetris condition led to fewer intrusive memories of the trauma film compared to no retrieval and no Tetris ($d = 1.00$), Tetris alone ($d = 0.84$), and retrieval alone ($d = 1.11$) conditions. There were no significant differences between the other three conditions (i.e., no retrieval and no Tetris, Tetris alone, retrieval alone). Furthermore, the frequency of intrusive memories declined significantly faster in the retrieval plus Tetris condition, compared to all other conditions. Again, no significant differences were found between the other three groups. Together, the findings of James et al. (2015) demonstrate
consistency with reconsolidation theory; visuospatial interference during the reconsolidation window resulted in fear memory attenuation, but the interference alone or the retrieval alone resulted in no change to the memory. Later research further tested this visuospatial interference paradigm’s basis in reconsolidation theory by replicating the first study in James et al. (2015) but with Tetris (and the equivalent amount of time sitting quietly for the control condition) occurring prior to memory retrieval (James et al., 2016). The results of this follow-up study demonstrated no significant differences between conditions, providing further support that reconsolidation mechanisms are involved in the visuospatial interference paradigm (James et al., 2016). These studies together provide support for the use of Tetris, and the visuospatial interference paradigm as a whole, to interfere with reconsolidation of fear memory. Furthermore, they demonstrate evidence that the mechanism of action of this paradigm is indeed through reconsolidation processes.

Clinical Applications

Iyadurai et al. (2018). The visuospatial interference paradigm has been tested for clinical use in blocking the consolidation of fear memories. In a study by Iyadurai et al. (2018), individuals presenting to an emergency department in a United Kingdom hospital within six hours of a motor vehicle accident were recruited and randomly assigned to either the experimental or control condition. Participants in the experimental condition were asked to briefly recount the worst moment of the accident, then play Tetris for approximately 20 minutes. Participants in the control condition simply completed an activity log of the entire day’s events for 20 minutes. Participants in both conditions then were instructed to record all intrusive memories of the accident in a journal for the next week. Follow-up assessment occurred at one-
week postintervention. A measure of distress due to intrusive memories was also administered at one-week and one-month postintervention. Results of the study demonstrated that playing Tetris following a motor vehicle accident predicted fewer intrusive memories ($d = 0.67$), a faster decline in the frequency of intrusive memories and less distress caused by intrusive memories one week following the accident ($d = 0.54$) compared to the control condition. No difference in distress due to intrusive memories was found at one-month postintervention. This study provides some evidence of the utility of Tetris for attenuating consolidation of fear memory; however, results have thus far failed to replicate using a trauma analog (Brühl et al., 2019).

Kessler et al. (2018). Despite mixed results targeting memory consolidation with the visuospatial interference paradigm, research has examined the efficacy of this paradigm for interfering with the reconsolidation of previously learned memories. In a study by Kessler et al. (2018), 20 inpatients with longstanding complex PTSD were asked to monitor their intrusive memories throughout their inpatient hospitalization (5 to 10 weeks). Once a week during their stay, they briefly retrieved a memory of a specific intrusion then played 25 minutes of Tetris. Results demonstrated that targeted intrusions decreased significantly compared to nontargeted intrusions. This study provides support for the use of a visuospatial interference paradigm for disruption of memory reconsolidation. More research is needed to understand the conditions in which this paradigm is most effective and to further develop it for clinical use.

**Ecological Validity**

Reconsolidation models state that reconsolidation processes exist as adaptive measures for the expedient updating of old memories with new, relevant information (Alberini & LeDoux, 2013). These processes are adaptive because the organism does not have to experience the same
event multiple times to learn new information. Instead, it can experience a similar event that triggers the old memory, and that memory can then be altered to incorporate this new information (Alberini & LeDoux, 2013). Based on this idea, reconsolidation models predict that fear-relevant memories of one event would be attenuated after exposure to a similar, but less fear inducing second event.

Weems et al. (2014). The study by Weems et al. (2014) demonstrated the ecological validity of memory reconsolidation models by testing this prediction in a natural setting. In this study, students in two separate samples who experienced Hurricane Katrina were asked to write down an account of the event. Later, following exposure to a second storm (Hurricane Gustav), the students were again asked to write down their account of Katrina. A significant decrease in negative memories of Katrina was predicted by low negative Gustav exposure in both samples. It was theorized that exposure to Gustav initiated recall of the memories of Katrina, and for those participants who did not have a highly negative experience with Gustav, the new safety information was incorporated into the old Katrina memory. This change in the original Katrina memory does not reflect the mere learning of new safety information, as the memories of Katrina themselves were altered to be less negative. Instead, the attenuation of the original memory suggests that memory reconsolidation processes changed that memory to match the new information presented by Gustav. The demonstration by Weems et al. (2014) that long-term memories can be updated without pharmacological intervention lends ecological validity to the memory reconsolidation models. When new information was presented that was relevant to the memory of Hurricane Katrina, this information was naturally incorporated into the original memory, thus allowing participants to quickly adapt to the new safety information.
Kredlow and Otto (2015). The ecological validity of memory reconsolidation models has also been demonstrated in a population exposed to the Boston City bombing (Kredlow & Otto, 2015). In this study, 113 undergraduates with varying degrees of exposure to the Boston City bombing were asked to answer questions about the bombing and describe it in as much detail as possible as a way of activating the memory (Time 1). Participants were then given either no interference task or were asked to read a negative, positive, or neutral story that was unrelated to the bombing. After one week (Time 2), the participants were given the same retrieval task as at Time 1. A significant decrease in memory details was found from Time 1 to Time 2, but only in the condition that read the negatively valanced story for their interference task at Time 1. The findings of Kredlow and Otto (2015) support the ecological validity of reconsolidation theory by showing that an interference task after activation of a real traumatic memory results in a decrease in the declarative content of that memory. Importantly, the emotional valence of the interference task (e.g., the negative story) determined whether reconsolidation interference was successful. It is possible that matching interference task emotional valence with the emotional valence of the target memory represents a contextual boundary condition for the interference of reconsolidation for declarative content in memories. In short, it may be that reconsolidation processes may only be engaged for declarative memory content when the interfering stimulus triggers a similar emotional response as the activated memory. Although this finding has not been demonstrated in studies testing reconsolidation interference of emotional content, other studies have supported the existence of boundary conditions under which a memory may become more or less susceptible for erasure (e.g., Björkstrand et al., 2015; Bustos et al., 2009; Dębiec et al., 2006; Diaz-Mataix et al., 2013; Forcato et al., 2009; Frankland et al., 2006; Lee, 2010; Lee et al., 2006; Monfils et al., 2009; Nader et al., 2000; Oyarzún et al., 2012; Robinson & Franklin, 2010;
Schiller et al., 2010; Sevenster et al., 2013; Sevenster et al., 2014; Suzuki et al., 2004; Winters et al., 2009). Any study seeking to interfere with memory reconsolidation processes may need to take these boundaries into account in order to successfully activate and attenuate a memory.

Boundaries of Reconsolidation

Fear memory attenuation using the retrieval-extinction and visuospatial interference paradigms has been demonstrated in studies showing both short- and long-term persistence with self-report, psychophysiological, and fMRI measures (Björkstrand et al., 2015; Hu et al., 2018; Iyadurai et al., 2018; James et al., 2015; Kessler et al., 2018; Maples-Keller et al., 2017; Oyarzún et al., 2012; Schiller et al., 2010; Siegesleitner et al., 2019). However, similar findings have not been found in every case (Brühl et al., 2019; Hu et al., 2018; James et al., 2015; James et al., 2016; Siegesleitner et al., 2019; Soeter & Kindt, 2011), leading researchers to examine the boundary conditions under which reconsolidation takes place. The most studied of the parameters of reconsolidation is the period of time after memory retrieval. Animal and human studies both indicate that reconsolidation lasts no longer than six hours after the memory is activated (Björkstrand et al., 2015; Monfils et al., 2009; Nader et al., 2000; Schiller et al., 2010). Any attempts at interference before memory activation or after this window is not believed to engage the reconsolidation process and will not result in persistent changes to memory (Björkstrand et al., 2015; James et al., 2015; James et al., 2016; Monfils et al., 2009; Nader et al., 2000; Schiller et al., 2010).

The cues used to activate a memory cannot present information that is too indirectly related to the targeted memory. A study by Dębiec et al. (2006) created an associated memory network in rats using second-order fear conditioning. This type of fear conditioning begins by
creating a learned association between a stimulus (CS1) and a response (CR), then creates a further association between CS1 and a second stimulus (CS2). In this way, a direct association is formed between CS1 and CR, and an indirect association is formed between CS2 and CR. Results indicated that memory activation of the CS1-CR association and subsequent reconsolidation blockade disrupted only that association without affecting the CS2-CR association. These findings demonstrate that, in order to attenuate an entire associative memory network, each individual memory needs to be activated and have its reconsolidation disrupted, but when targeting a single memory with reconsolidation interference, other related memories will not become impaired (Dębiec et al., 2006).

The cue that activates the memory cannot last for too long or too short of a duration (Bustos et al., 2009; Lee et al., 2006). A cue that is presented for too short of a time will not activate reconsolidation, but a cue that lasts too long will begin extinction, and attempts to disrupt reconsolidation after the cue will block consolidation of the extinction memory instead. The length of time the cue must be presented to the subject is believed to vary based on the age and strength of the consolidated memory. Older memories have been more thoroughly consolidated into LTM and are more likely to have experienced greater LTP (Frankland et al., 2006). These memories are resistant to destabilization unless the activation cue is presented for a longer period of time (Frankland et al., 2006). Stronger memories also require longer activation cue durations, although some studies have shown that strongly trained memories become more susceptible to destabilization over time (Frankland et al., 2006; Robinson & Franklin, 2010). Memories that have been strongly trained, as traumatic memories are believed to be, have experienced considerable LTP even if they are more recent (Suzuki et al., 2004).
Using a contextual fear conditioning paradigm followed 24 hours later by systematic adjustment of activation cue lengths prior to administration of protein inhibitors, animal models have determined that an activation cue for a remote or strongly trained memory should take approximately 10 minutes. Shorter cues (i.e., 0, 1, 3, or 5 minutes) were shown to be less effective at initiating reconsolidation processes for these memories, as demonstrated by return of fear when the mice were re-exposed to the training context. Longer cues (i.e., 30 minutes) engaged extinction processes instead, resulting in a decrease in the fear response over the course of the cue but impaired retention of the new safety information 24 hours later (Suzuki et al., 2004). Research into the boundaries of activation cue duration in humans has thus far only been conducted using recently consolidated memories (Hu et al., 2018). In this study, reminder cues of shorter duration (i.e., 1 second, 4 seconds) were most effective at triggering destabilization of memories formed 24 hours earlier. This research provides important information regarding destabilization of recent memories in humans, but more research is needed to discover the appropriate activation cue duration for older, stronger, and more complex memories.

**Novelty**

Some research suggests that reconsolidation of remote and strongly trained memories can be triggered by exposure to novel stimuli during memory retrieval. Winters et al. (2009) used the spontaneous object recognition paradigm for rats, in which rats are allowed to explore two objects in opposite arms of a Y-shaped apparatus and later have to choose between one of the familiar objects and a novel object. In this study, mice were released into the apparatus in order to explore the two stimuli. Later, a short (~2 minute) memory activation session was conducted. In the activation session, rats were injected with an NMDA-receptor antagonist and released
back into the apparatus either in the exact same context as the learning phase or a context that was similar except for the addition of a Styrofoam floor insert that extended into each arm of the apparatus. Twenty-four hours later, all rats were placed back into the apparatus in the original context, with one of the familiar stimuli in one arm of the maze and a new stimulus in the other arm. Reconsolidation interference was determined by the ratio of time the rats spent exploring the familiar stimulus compared to the novel stimulus. Results from the study showed that the experience of the novel context during the activation phase predicted the rats spending equal amounts of time exploring the familiar vs. the novel stimulus in the later trial. These findings suggest that the novel context during the activation trial initiated reconsolidation interference of the memory of the familiar stimulus. These findings were demonstrated even when the memory was strong (the learning session was conducted three times prior to the activation trial) or if the memory was remote (the interval between the learning and activation sessions was 48 hours). Similar results were not found in rats that did not experience the novel stimulus. These findings are similar to studies with humans that show that reconsolidation interference is facilitated by introducing new information during memory activation (Gotthard & Gura, 2018; Sevenster et al., 2014).

It has been theorized that memory reconsolidation is a natural memory update mechanism, so introducing novel or contradictory information during memory activation may trigger the process (Díaz-Mataix et al., 2013; Sevenster et al., 2013). This theory is supported by studies that show that reconsolidation interference does not occur when the activation cue for a lab-trained fear memory is exactly the same as a trial of fear conditioning (i.e., the activation cue includes both the CS and the CR; Forcato et al., 2009; Morris et al., 2006; Pedreira et al., 2004).
Instead, it is believed that it is the new information of the CR not occurring with the CS that triggers the reconsolidation process (Forcato et al., 2009).

Research has also shown that memory reconsolidation does not occur after novel information relevant to the original memory has been presented multiple times (Rodriguez-Ortiz et al., 2005). In this study, the effect of anisomycin-facilitated reconsolidation interference was strongest when novel information was presented. However, when anisomycin was administered after the new information had been presented multiple times so that learning had reached an asymptote, reconsolidation was no longer triggered by memory retrieval, and the consolidated memory remained intact (Rodriguez-Ortiz et al., 2005). Although several studies suggest that novelty may be a boundary condition for inducing memory reconsolidation, novelty alone has been shown to be unsuccessful at triggering these processes (Hardwicke et al., 2016). Instead, it has been suggested that the key component for triggering memory reconsolidation may not be novelty, but prediction error during presentation of the retrieval cue (see Exton-McGuinness et al., 2015 for a review).

Prediction Error

The role of prediction error in memory reconsolidation has been gaining traction as a fundamental part of reconsolidation theory (Exton-McGuinness et al., 2015). Prediction error occurs when a cue triggers retrieval of a previously stored memory in order to predict the next event or series of events, but that prediction does not match what actually occurs (Rescorla & Wagner, 1972). Neurological evidence has suggested that the left hippocampus differentially activates when a retrieval cue contains a prediction error compared to a cue that matches expectations (Forcato et al., 2016). This differential activation was shown to correspond to
memory updating (Forcato et al., 2016). However, the use of retrieval cue prediction error to destabilize a memory is delicate; although a single prediction error has been shown to lead to reconsolidation processes, multiple prediction errors may lead to new memory formation through extinction (Sevenster et al., 2014).

Despite the delicate nature of the retrieval cue with prediction error, research has demonstrated that such a cue may lead to memory destabilization and allow for reconsolidation interference using the retrieval extinction paradigm (Sinclair & Barense, 2018). In the Sinclair and Barense (2013) study, participants were shown 18 videos on Day 1 (e.g., a baseball player hitting a home run). One day later, they were randomly assigned to either the experimental or control condition. For the experimental condition, participants were shown the Day 1 videos again as a retrieval cue for their memory of watching the video on Day 1. Some of these retrieval cue videos were played in full, others were interrupted (i.e., stopped) before the conclusions. Which videos were played in full and which were interrupted was random for each participant. Following each retrieval cue video and a 7-minute delay, participants watched “interference videos” that were semantically related to the Day 1 videos, but contained new content (e.g., a video of a different baseball player hitting a ball that gets caught by a fan). For the control condition, all procedures were the same as for the experimental condition, except the interference videos were presented prior to the retrieval cues. One day following Day 2 (Day 3), all participants were interviewed about their memories of each film. Results demonstrated that presentation of the interference video following the retrieval cue video and 7-minute delay (but not before the retrieval cue and delay) on Day 2 resulted in retroactive interference of participants’ memory of the Day 1 videos. These data suggest that the retrieval cues successfully destabilized the memory of the Day 1 videos, thus allowing for memory modification via the
interference videos. More importantly, the results also demonstrated that the interrupted (i.e., prediction error) videos led to more modification of the Day 1 video memories. Specifically, more information in the Day 3 memory of the Day 1 videos was either entirely false or misremembered as part of the Day 1 videos when the information was actually from the Day 2 interference videos. Furthermore, based on independent ratings of the videos, the more subjectively surprising the video the stronger it predicted memory modification, suggesting that stronger prediction errors led to increased destabilization and subsequent interference (Sinclair & Barense, 2018). This study successfully demonstrates that prediction error may be essential for memory destabilization and updating in a retrieval-extinction paradigm. To date, no research has examined whether these findings may translate for clinical use.

Reconsolidation Interference as a Potential PTSS Treatment

Research has examined memory consolidation as a potential target of interventions to prevent the development of PTSD; however, interfering with the initial consolidation of a traumatic memory has limitations. The issues of resources and timing make targeting consolidation extremely difficult in many cases. Memory consolidation occurs immediately following an event, so targeting consolidation of a traumatic memory would require the resources to provide treatment to people within 6 hours of a traumatic event (McGaugh, 1999). For individual traumatic events such as rape, providing immediate mental health care can be problematic as the victim may not seek out help until after the memory has consolidated (Campbell et al., 2001; Williams, 1984). For large scale traumatic events such as natural disasters, the resources required for mass interventions for the entire affected population may not be available (World Health Organization, 2003). In fact, estimates from the American Red Cross
state that disaster-response aid takes between 24 and 48 hours to mobilize (American Red Cross, 2010). These logistical issues make blocking memory consolidation impractical as a measure to prevent the development of PTSD.

Even if the necessary resources were available promptly after a traumatic event, research has shown that immediate interventions may not actually be beneficial to the affected individual. One study by Schiller et al. (2008), tested the effectiveness of consolidation interference of fear memories in human subjects. On Day 1, participants were first conditioned to fear a specific stimulus by pairing its presentation with a mild electrical shock to the wrist. Fear response, measured by skin conductance, was significantly different from zero immediately following this conditioning, demonstrating that fear of the stimulus was learned. Next, that learned fear response was extinguished during the consolidation window to test if extinction training during that window would interfere with consolidation of the conditioned fear response. At the end of extinction training, the learned fear response was no longer significantly different from zero, demonstrating that fear of the stimulus was successfully extinguished. One day later (Day 2), participants returned to assess for spontaneous recovery of the learned fear response. Comparing fear responses from the end of extinction training on Day 1 to the responses from the test for spontaneous recovery on Day 2 found a significant difference between the two, demonstrating that spontaneous recovery of the learned fear response occurred despite the attempted memory consolidation interference. These results imply that extinguishing fear during the initial fear memory consolidation window does not interfere with the consolidation of the memory. Instead, this intervention merely engaged extinction mechanisms, which resulted in initial extinction of the learned fear response followed by spontaneous recovery of that response.
Other studies have shown that immediate treatment following a traumatic event may actually be detrimental to a person’s mental health. Using critical incidence stress debriefing (CISD) immediately following trauma has been shown to increase PTSD symptoms in trauma survivors (Bisson et al., 1997; Wei et al., 2010). It is possible that CISD interferes with the initial consolidation of a traumatic memory, which may disrupt natural recovery and exacerbate the development of PTSD symptoms (McNally et al., 2003). Despite promising results from studies like Iyadurai et al. (2018), the possibility of pharmacological and psychotherapeutic interventions during traumatic memory consolidation damaging victims of trauma must be considered. Developing an intervention that utilizes reconsolidation mechanisms after PTSD symptoms have developed may be a safer and more beneficial strategy.

Research into interfering with reconsolidation mechanisms in fear memories often uses a pharmacological blockade of reconsolidation (Alberini & LeDoux, 2013; Brunet et al., 2008; Brunet et al., 2010; Ishikawa et al., 2016; Muravieva & Alberini, 2010; Nader et al., 2000; Tronson et al., 2006; Wood et al., 2015). Research has produced mixed results by targeting fear memories with drugs like propranolol, and it has been suggested that pharmacological intervention is not capable of addressing the complexities of real traumatic memories (Ishikawa et al., 2016; Muravieva & Alberini, 2010; Wood et al., 2015). Utilizing behavioral techniques to engage the reconsolidation process allows for more flexibility to personalize treatments for individual differences in traumatic experiences and PTSD presentation. Research has shown that behavioral interventions are effective at targeting fear memories and the boundaries under which these interventions may be successful have been outlined. Adapting current PTSD treatments so that they incorporate memory destabilization and reconsolidation processes may therefore result in a highly effective intervention.
The Present Study

The present study seeks to translate the current reconsolidation literature into a behavioral intervention for clinical use in treating PTSS. A sample presenting with PTSS was asked to write a complete and detailed trauma narrative. One week later, participants were randomly assigned to one of two conditions. For the Prediction Error condition, participants listened to the audio recording of their narrative once, but it was interrupted (i.e., stopped and not resumed) prior to completion. The recording was followed by a 7-minute wait, then they played 25 minutes of Tetris followed by listening to the audio recording of their narrative repeatedly until habituation occurred. Requiring habituation following the Tetris interference is intended to further interfere with reconsolidation of the fear memory by replacing fear information with safety information learned during the exposure. For the Full Retrieval Control condition, participants listened to the audio recording of their narrative once in full followed by a 7-minute wait, then played 25 minutes of Tetris followed by listening to the audio recording of their narrative repeatedly until habituation occurs. Inclusion of this control condition allows for comparison with the Prediction Error condition to test whether prediction error during the memory activation cue is necessary to initiate reconsolidation processes. One week later, all participants returned to the lab for a follow-up assessment.

Hypotheses

Although other studies have demonstrated reconsolidation interference without explicitly targeting prediction error (e.g., Schiller et al., 2010), that research is mixed (e.g., Soeter & Kindt, 2011). The literature reviewed suggests that prediction error during the memory activation cue is
a necessary boundary condition for successfully engaging reconsolidation processes. Therefore, it is hypothesized that:

H1  The Prediction Error condition will show a decreased SUDS response during activation from Day 2 to Day 3 compared to the Full Retrieval Control condition.

H2  The Prediction Error condition will show a greater decrease in overall PTSS from Day 2 to Day 3 compared to the Full Retrieval Control condition.

H3  The Prediction Error condition will show a greater decrease in intrusion symptoms from Day 2 to Day 3 compared to the Full Retrieval Control condition.

H4  The Prediction Error condition will show a greater decrease in psychophysiological reactivity from Day 2 to Day 3 compared to the Full Retrieval Control condition.
Participants from this study were recruited from a mass testing pool of undergraduate students enrolled in an introductory psychology course at a large midwestern United States university ($n = 60$). Study participants were randomly assigned into two conditions, stratified by sex and Day 1 Questionnaire Phase PCL-5 score group (i.e., subthreshold = 20 – 30; threshold = 31 – 40; moderate = 41 – 50; severe = 51 or higher), so that the two conditions contained a proportional number of males and females and individuals with varying levels of symptom severity. Eligibility for the current study was determined by presence of PTSS, as evidenced by total scores on the PTSD Checklist for DSM-5 (PCL-5; Blevins et al., 2015; Bovin et al., 2015), and concomitant endorsement of a primary traumatic experience occurring after age 14, as evidenced by the participant’s response on the Life Events Checklist for DSM-5 (LEC-5; Weathers et al., 2013). Eligibility criteria was assessed both during mass testing and during the Day 1 Questionnaire Phase. A cutoff score of 31 to 33 is suggested as a mark of PTSD (Bovin et al., 2015). This study expected that the effects of reconsolidation interference were present in a subclinical sample, so a score of 20 was used as a cutoff. This score corresponds with an average score of at least one on all of the items on the PCL-5. Furthermore, in accordance with DSM-5 criteria for PTSD, participants were only eligible for the study if their primary traumatic event occurred prior to mass testing by one month or greater, as reported on the PCL-5. Other
exclusion criteria include heart conditions that may interfere with measures of HR, such as certain arrhythmias, and experience of a traumatic event during the course of the study. Finally, participants who did not demonstrate evidence of memory activation on at least one measure (i.e., SUDS, SC, HR) during the Day 2 Activation Phase were excluded.

To determine the sample size, a power analysis was conducted using G*Power (Erdfelder et al., 1996). Based on Brunet et al. (2008), an effect size of $d = 0.92$ was used. Setting alpha to .05 and power to .80, a total sample size of 20 would be needed to detect an effect. Considering the possibility of a smaller effect size, as well as the fact that power analysis does not account for many factors that affect power (e.g., reliability of measures), the sample size for this study was 20 participants per condition (i.e., 40 total participants) in order to account for any unanticipated loss of power.

**Risk, Consent, and Confidentiality**

Considering that there is some risk involved for participants to recount their previous traumatic experiences, strict consent procedures are necessary. All participants were informed that they would be expected to write about their primary traumatic event and that they would be asked to emotionally engage with this memory. They were also informed that research assistants would be reading their scripts and recording audio of these scripts being read aloud, and that they (the participant) would be asked to listen to this recording multiple times. All data was kept separately from identifying information in a locked filing cabinet or password protected electronic file. Finally, arrangements were made with the Psychological Services Center for any participants experiencing significant distress to be fast-tracked into therapy services.
Measures

Outcome Measures

Posttraumatic Stress Symptoms

The PCL-5 is a 20-item self-report measure of PTSS and symptom severity (Bovin et al., 2015). The measure assesses DSM-5 criterion A, the presence of criterion B, C, and D symptoms, the length of time that the symptoms have been present (criterion E), and the level of distress the symptoms cause (criterion F). The initial PCL was published in 1993 and contained only 17 items (Weathers et al., 1993). The current version of the scale has been updated to reflect the PTSD criteria in the newest edition of the DSM (Blevins et al., 2015). Respondents are asked to rate the degree to which they have experienced each item over the last month on a scale from 0 (not at all) to 4 (Extremely; Blevins et al., 2015). The version of the PCL-5 used in this study was adapted to assess for PTSS and symptom severity over the past week and was tied to the participant’s primary traumatic event, using the following prompt:

Below is a list of problems that people sometimes have in response to a very stressful event. Keeping your worst event in mind, please read each problem carefully and then choose one of the numbers to indicate how much you have been bothered by that problem in the past week.

In the past week, how much were you bothered by:

Using a veteran sample, a total score of 31 to 33 has been shown to be the optimally efficient cutoff score to maximize specificity (.69) and sensitivity (.88) of PTSD diagnosis. (Bovin et al., 2015). The PCL-5 has shown good psychometric properties in military and community populations (Armour et al, 2015; Biehn et al., 2013; Bovin et al., 2015; P. Liu et al., 2014), with the initial psychometric analysis demonstrating high test-retest reliability ($r = .82$),
internal consistency ($\alpha = .94$), and convergent and discriminant validity ($r = .74-.85$ and $r = .31-.60$ respectively; Blevins et al., 2015).

**Sleep**

Research has suggested that sleep may be an important factor that influences memory consolidation and reconsolidation (see Stickgold & Walker, 2007), and sleep problems are one symptoms of PTSD (American Psychiatric Association, 2013). Therefore, a measure of sleep was included as a covariate in the current study. The Pittsburgh Sleep Quality Index (PSQI) is a 19-item self-report questionnaire that assesses sleep quantity and quality (Buysse et al., 1989). The original measure assessed sleep over the past month (Buysse et al., 1989); however, the version used in the current study has been adapted to assess sleep over the past week (Dietch et al., 2016). The PSQI measures seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction (Dietch et al., 2016). It has been found to have good internal consistency ($\alpha = .83$; Buysse et al., 1988), good test-retest reliability ($r = 0.85$; Buysse et al., 1988), and adequate validity (Buysse et al., 1988; Dietch et al., 2016). The measure has demonstrated acceptable diagnostic sensitivity and specificity for distinguishing between good and poor sleepers (Buysse et al., 1988) and in diagnosing insomnia (Dietch et al., 2016).

**Psychophysiological Arousal**

Skin conductance response (SC) and heart rate (HR) are the most commonly used psychophysiological measures in human studies of memory reconsolidation interference (Björkstrand et al., 2015; Brunet et al. 2008; Hu et al., 2018; Oyarzún et al., 2012; Schiller et al.,
In the study by Brunet et al. (2008), these two measures also showed the strongest effect sizes \((d = 1.23\) and \(d = 0.92\), respectively), compared to electromyogram \((d = 0.29\). Because of these findings and the preference for SC and HR in the literature, SC and HR were used in this study to measure psychophysiological arousal in association with recovery of fear.

**Skin conductance response.** Skin conductance response (SC) is a measure of changes in electrodermal conductivity that are associated with autonomic arousal (LaBar et al., 1998). SC is the most common method for measuring spontaneous recovery of fear in human studies of memory reconsolidation interference (e.g., Björkstrand et al., 2015; Brunet et al., 2008; Hu et al., 2018; Oyarzún et al., 2012; Schiller et al., 2010; Soeter & Kindt, 2012; Wood et al., 2015). Studies have demonstrated a relationship between SC and emotional memory activation, as well as between SC and amygdalar function as measured with PET or fMRI (Furmark et al., 1997; Hamann et al., 1999; LaBar et al., 1998). These studies indicate that SC is a valid and reliable measure of emotional activity and arousal and provide support for its use as a measure of fear response.

**Heart rate.** Heart rate (HR) is a common measure of fear response that has been reliably used for decades (Lang et al., 1970; Sartory et al., 1977). This measure is commonly used in human pharmacological studies of memory reconsolidation interference (Brunet et al. 2008; Wood et al., 2015). Research has demonstrated highly elevated HR in people with PTSS when they are exposed to traumatic imagery (Orr et al., 2002; Pitman et al., 1987). These studies support the use of HR as a valid measure of fear response in a human PTSS sample.
Subjective Distress

The Subjective Units of Distress Scale (SUDS) was developed by Wolpe (1973) as a self-report measure of anxiety. The respondent is asked to rate their anxiety on a scale from 0 (absolutely calm) to 100 (the worst anxiety you have ever experienced; Thyer et al., 1984). SUDS has been shown to have concurrent validity as a measure of anxiety with HR ($r = .39$, $p < 0.05$) and hand temperature (left hand $r = .85$, $p < 0.01$; right hand $r = 0.83$, $p < 0.01$; Thyer et al., 1984).

Other Measures

Demographics

The demographic questionnaire assessed sex. This information was used to stratify the random assignment to the three conditions. Participants were also asked to identify their race, age, marital status, and previous mental health diagnoses, including diagnosed heart conditions to determine eligibility.

Traumatic Events

The Life Events Checklist for DSM-5 (LEC-5) is a 15-item self-report measure of potentially traumatic events that the respondent may have experienced in their lifetime (Weathers et al., 2013). Participants are asked to respond to each item with all relevant responses that include 0 (it happened to me), 1 (witnessed it), 2 (learned about it), 3 (part of my job), 4 (not sure). In the current study, the LEC-5 was modified to assess only for events that have occurred more than one month prior, using the following prompt.
Listed below are a number of difficult or stressful things that sometimes happen to people. For each event, *mark all relevant responses that apply to you* to indicate that:

(0) it *happened to you* personally;
(1) you *witnessed it* happen to someone else;
(2) you *learned about it* happening to a close family member or close friend;
(3) you were exposed to it as *part of your job* (for example, paramedic, police, military, or other first responder); or
(4) you’re *not sure* if it fits.

Be sure to consider only events that have occurred *greater than one month ago* as you go through the list of events.

The LEC-5 is an updated version of the Life Events Checklist (LEC) that is designed to better reflect DSM-5 PTSD criterion A. The LEC has demonstrated adequate temporal stability and good convergent and criterion validity (Gray et al., 2004).

**Procedure**

**Day 1**

Participants began by completing a battery of baseline questionnaires including the demographic questionnaire, the LEC-5 immediately followed by the PCL-5, and the PSQI in random order (the Day 1 Questionnaire Phase). Participants who scored above a 20 on the PCL-5, indicate a primary traumatic event occurring greater than one month ago but after age 14, and report no heart conditions were randomly assigned and stratified by sex and PCL-5 severity group into one of two conditions. Participants in both conditions were asked to record their current SUDS rating, then write their full trauma narrative for a minimum of 30 minutes (the Day 1 Writing Phase), providing current SUDS ratings every 5 minutes. Following the writing task, participants were then asked for their current SUDS ratings again. They were then dismissed.
Writing Task

The writing task used in written exposure therapy (WET) is an adaptation of the Pennebaker writing task (Sloan et al., 2012). Both tasks ask participants to imagine the event that causes them the most distress and write about the event in as much detail as possible (Pennebaker & Chung, 2011; Sloan et al., 2012). The Pennebaker writing task is a widely used paradigm that has been shown to be a valid and reliable form of exposure (Esterling et al., 1999; Pennebaker & Chung, 2011). A study by Danoff-Burg et al. (2010) demonstrated that writing about a stressful event in an emotionally meaningful way was associated with decreases in depression and perceived stress in both expressive writing and narrative writing conditions. In a study of rape victims, it was found that participants who used a moderate level of personalization during the writing task and included greater detail showed a significant decrease in symptoms of social anxiety and dysphoria (Brown & Heimberg, 2001). The Pennebaker writing task has also been used successfully in a population of people diagnosed with PTSD to decrease trauma related distress and facilitate posttraumatic growth (Smyth et al., 2008). The writing task used in WET has also been shown to be an effective form of exposure compared to a wait-list control (Sloan et al., 2012), and not inferior to cognitive processing therapy, another active trauma-focused treatment (Sloan et al., Resick, 2018). Although both the Pennebaker writing task and its derivative, WET, have been shown to be effective exposures for treating PTSS, the current study used the writing prompt from WET as that prompt is tied to a specific traumatic event, unlike the prompt used for the Pennebaker task. The WET prompt encourages participants to think deeply about their traumatic event and asks specifically for them to express emotional content. In the current study, participants read the prompt out loud to ensure complete understanding. The
writing task was used to generate a trauma narrative to be read and recorded in its entirety by a single, consistent female research assistant between Day 1 and Day 2.

Day 2

All participants were to return to the lab one week following Day 1. Participants began Day 2 by completing a battery of questionnaires, including the LEC-5, PCL-5, and the PSQI (the Day 2 Questionnaire Phase). For Day 2, the LEC-5 was adapted to ask about the past week only. Any participant who reported experiencing a new traumatic event in the past week on the LEC-5 was debriefed and dismissed. All participants were then connected to HR and SC wireless BIOPAC equipment. For all conditions, participants who did not demonstrate arousal indicative of memory activation during the Day 2 Activation Phase (see below) on at least one measure (i.e., increased HR, SC, SUDS scores) were dismissed and excluded from the study.

For HR, researchers used alcohol wipes to slightly abrade and clean the left shoulder (left arm), right shoulder (right arm) and left upper quadrant of the abdomen (left leg). Once each area dried, one lead was placed on each location, so that the lead was flush with the skin. A (+-) electrode was placed on the left shoulder (left arm), a (--) electrode on the right shoulder (right arm), and a (++) electrode on the left upper quadrant of the abdomen (left leg).

For SC, researchers began by slightly abrading and cleaning the participant’s distal phalanges on their second and fourth fingers of their nondominant hand. A unibase electrolyte paste was inserted into two silver-silver chloride cup electrodes. The positive electrode was then clamped to the volar surface of the distal phalanx of the second finger. The negative electrode was clamped to the volar surface of the distal phalanx of the fourth finger.
The SC and HR electrodes were connected to a wireless transmitter strapped to the participant’s nondominant wrist. All electrodes were then calibrated. Participants were be habituated until SC and HR were stable (the Day 2 Habituation Phase). Following habituation, baseline readings were recorded for five minutes (the Day 2 Baseline Phase).

**Full Retrieval Control Condition**

Following the Day 2 Baseline Phase, participants in the Full Retrieval Control condition listened to the full recording of their trauma narrative once (the Day 2 Activation Phase). During the Day 2 Activation Phase, participants were asked to close their eyes and allow themselves to experience any emotions that occurred. Their SUDS ratings were recorded at the beginning and end of this phase, including a retrospective recording of their highest SUDS. There was then a seven-minute wait to allow the reconsolidation window to open. After the seven-minute break, participants then played 25 minutes of Tetris (the Day 2 Distraction Phase). Immediately following, they continued to listen to their full audio recorded narrative repeatedly and without stopping (the Day 2 Extinction Phase). Their SUDS ratings were recorded at the beginning, end, and every 5 minutes during this phase. Once their SUDS ratings decreased by half from their highest to their baseline, the psychophysiological recording equipment was removed. They were then dismissed.

**Prediction Error Condition**

Following the Day 2 Baseline Phase, participants in the Prediction Error condition completed the Day 2 Activation Phase; however, their recording stopped right as the most distressing part of the narrative begins. The most distressing part of the narrative was determined
by counting the number of self-referencing words (e.g., “I”, “my”) and positive and negative emotion words. These assessments have been used in multiple studies to determine the degree to which participants engage in a writing task (e.g., Brown & Heimburg, 2001; Pennebaker, 1997).

Similar to the Full Retrieval Control condition, participants in the Prediction Error condition were asked to close their eyes and allow themselves to experience any emotions that occurred during the Day 2 Activation Phase. SUDS ratings were recorded at the beginning and end of this phase, including a retrospective recording of their highest SUDS. Following this phase, there was a seven-minute break to allow the reconsolidation window to open, then participants completed the same Day 2 Distraction and Extinction Phase protocols as the Full Retrieval Control condition. They were then dismissed.

**Day 3**

All participants were to return to the lab one week following Day 2. Participants began Day 3 by completing a battery of questionnaires, including the LEC-5, PCL-5, and the PSQI (the Day 3 Questionnaire Phase). Similar to Day 2, the LEC-5 on Day 3 was adapted to ask about the past week only and any participant that reported experiencing a new traumatic event in the past week was debriefed and dismissed. Following the questionnaires, participants were connected to HR and SC wireless BIOPAC equipment following the same protocol as described for Day 2. All participants then followed the same Habituation and Baseline procedures as on Day 2 (the Day 3 Habituation Phase and the Day 3 Baseline Phase, respectively). Following the Day 3 Baseline Phase, all participants listened to the audio recording of their full trauma narrative one time (the Day 3 Activation Phase). SUDS ratings were recorded at the beginning and end of this phase,
including a retrospective recording of their highest SUDS. The psychophysiological recording equipment was then removed. Participants were debriefed and dismissed.

See Figure 1 for a flow chart of the procedure.

Figure 1. Flow chart of the procedure process.
CHAPTER 3
DATA ANALYSIS

Data Screening

All data was assessed for patterns of missingness. If missing data was found to be missing completely at random (MCAR) or missing at random (MAR) and less than 1% of data was missing, mean substitution was used to impute missing values. If missing data was found to be MCAR or MAR and 1% to 5% of data was missing, multiple imputation was used to impute missing values. Multiple imputation substitutes multiple potential values for a missing data point and averages the values together to estimate a likely value for the missing data (Rubin, 1987). This technique allows for preservation of sample size and statistical power while providing unbiased results (McCleary, 2002; Sterne et al., 2009). The number of imputations was determined by the fraction of missing data in the sample (Bodner, 2008).

All assumptions for multivariate analyses were tested. Multivariate normality was established by examining the univariate normality of each variable as well as the linearity and homoscedasticity of each variable pair. The distribution of the residuals for each analysis was also examined for normality. All variables were also examined for multicollinearity. Bootstrapping was used in all analyses to obviate concerns about normality.

All variables were examined for extreme univariate outliers (i.e., outliers three times or greater than the interquartile range). If extreme outliers were found and there was no need for correction of clerical error (e.g., a value of 20 was accidently entered as a value of 200), then the
extreme outlier was winsorized. Multivariate outliers were assessed using Mahalanobis
distances. Values contributing to extreme multivariate outliers was also winsorized if there was
no need for correction of clerical error.

Overview of Analyses

For a full description of originally proposed analyses, please see Appendix A. All
hypotheses were tested using planned contrasts in the context of repeated measures ANCOVAs
controlling for sleep quantity and quality (i.e., mean PSQI scores during the Day 2 and Day 3
Questionnaire Phases; see Table 1).

For the first ANCOVA, the dependent variables were the SUDS ratings, with condition
as the between-subjects variable and time (i.e., the beginning of the Day 1 Writing Phase, highest
during the Day 1 Writing Phase, the beginning of the Day 2 Activation Phase, highest during the
Day 2 Activation Phase, the end of the Day 2 Activation Phase, the beginning of the Day 3
Activation Phase, highest during the Day 3 Activation Phase) as the within-subjects variable.
Planned contrasts were used in the context of the first ANCOVA to conduct paradigm checks,
randomization checks, and to test hypotheses H1.

For the second ANCOVA, the dependent variables were PCL-5 scores, with condition as
the between-subjects variable and time (i.e., the Day 1, Day 2, Day 3 Questionnaire Phases) as
the within-subjects predictor. Planned contrasts were used in the context of the second
ANCOVA as randomization checks and to test hypothesis H2.

For the third ANCOVA, the dependent variables were PCL-5 intrusion subscale scores,
with condition as the between-subjects variable and time (i.e., the Day 1, Day 2, Day 3
Table 1

Analyses as Originally Proposed

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose</th>
<th>Dependent Variables</th>
<th>Within-Subjects Variables (Time)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>T</em>-Tests</td>
<td>Randomization checks</td>
<td>Day 1 Questionnaire Phase mean LEC scores, mean PSQI scores, and gender</td>
<td></td>
</tr>
<tr>
<td>First ANCOVA</td>
<td>Paradigm checks; randomization checks; hypothesis H1</td>
<td>SUDS ratings</td>
<td>Beginning of the Day 1 Writing Phase; highest during the Day 1 Writing Phase; beginning of the Day 2 Activation Phase; highest during the Day 2 Activation Phase; end of the Day 2 Activation Phase; beginning of the Day 3 Activation Phase; highest during the Day 3 Activation Phase</td>
</tr>
<tr>
<td>Second ANCOVA</td>
<td>Randomization checks; hypothesis H2</td>
<td>Mean overall PCL-5 scores</td>
<td>Day 1, Day 2, and Day 3 Questionnaire Phases</td>
</tr>
<tr>
<td>Third ANCOVA</td>
<td>Randomization checks; hypothesis H3</td>
<td>Mean PCL-5 intrusion subscale scores</td>
<td>Day 1, Day 2, and Day 3 Questionnaire Phases</td>
</tr>
<tr>
<td>Fourth ANCOVA</td>
<td>Paradigm checks; randomization check; hypothesis H4</td>
<td>Mean HR</td>
<td>Day 2 Baseline Phase; Day 2 and Day 3 Activation Phases</td>
</tr>
<tr>
<td>Fifth ANCOVA</td>
<td>Paradigm checks; randomization checks; hypothesis H4</td>
<td>Highest SC</td>
<td>Day 2 Baseline Phase; Day 2 and Day 3 Activation Phases</td>
</tr>
<tr>
<td>Sixth ANCOVA</td>
<td>Hypothesis H4</td>
<td>SC slope</td>
<td>Day 2 and Day 3 Activation Phases</td>
</tr>
</tbody>
</table>

Note: Condition is the between-subjects variable for all tests and sleep quality/quantity is the covariate for all ANCOVAs.
Questionnaire Phases) as the within-subjects predictor. Planned contrasts were used in the context of the third ANCOVA as randomization checks and to test hypothesis H3.

For the fourth ANCOVA, the dependent variable was HR, with condition as the between-subjects variable and time (i.e., the Day 2 Baseline Phase, Day 2 Activation Phase, Day 3 Activation Phase) as the within-subjects variable. Planned contrasts were used in the context of the fourth ANCOVA as paradigm checks, a randomization check, and to partially test hypothesis H4.

For the fifth ANCOVA, the dependent variable was SC, with condition as the between-subjects variable and time (i.e., the Day 2 Baseline Phase, Day 2 Activation Phase, Day 3 Activation Phase) as the within-subjects variable. Planned contrasts were used in the context of the fifth ANCOVA as paradigm checks, a randomization check, and to partially test hypothesis H4.

For the sixth ANCOVA, the dependent variable was SC slope, with condition as the between-subjects variable and time (i.e., Day 2 Activation Phase, Day 3 Activation Phase as the within-subjects variable. Planned contrasts were used in the context of the sixth ANCOVA as a further test of hypothesis H4.
CHAPTER 4
DISSENTATION PROPOSAL AMENDMENT FOR CHANGES
DUE TO THE COVID-19 PANDEMIC

Due to the state-wide stay-at-home order and the closure of the Northern Illinois University campus, data collection for this doctoral dissertation research was halted indefinitely (all in-person data collection was officially halted on March 19, 2020). At the time of this unexpected end to data collection, only five participants met all inclusion criteria and had completed all three days of data collection. To ensure continued, uninterrupted progress in the Northern Illinois University Clinical Psychology Doctoral Program while maintaining the integrity and utility of this doctoral dissertation, the data from these five participants were thoroughly examined using a single-case design (see Gast & Spriggs, 2009). Although this study was not originally created under a single-case design, data from the primary outcome measures (i.e., heart rate, skin conductance) were incidentally collected in a way that fully satisfies the requirements of such a design. Data from secondary outcome measures (i.e., SUDS, PCL-5 scores) were less suited to such a design, and as such, interpretation of the results of these measures is limited.

Despite the added limitation for secondary measures, the analytical changes required to switch this study to a single-case design have a substantial benefit beyond the practical necessities resulting from the COVID-19 global pandemic. Translating findings from basic science to inform clinical intervention is a long, iterative process. As such, there is considerable
benefit to utilizing study methods that allow for small, quick data collections and analysis of the effect of the intervention within individuals. This design may allow researchers to pursue a program of research where data can be quickly collected and examined thoroughly for possible points of failure of the intervention, then appropriate data-driven changes to the intervention can be made and tested, ad nauseum. Considering the iterative nature of translational science, any study method that allows for rapid progression through iterations of intervention design is preferable to the time-consuming larger-scale studies required to validate an intervention once created. It is my view that a single-case design is therefore more appropriate for the purposes of this dissertation and should have been the proposed design initially. Furthermore, considering that data from the primary measures meet all requirements for a single-case design and data from secondary measures can be tentatively examined using such a design, I assert that no further data needed to be collected to address the questions proposed by this dissertation.

Brief Overview of the Original Method

To facilitate understanding of changes made to this study’s analytic strategy, a brief overview of the study’s design is presented.

All participants completed three days of data collection (see the Figure 1 for a visual representation). All three days began with completion of the battery of questionnaires (the Day 1, Day 2, and Day 3 Questionnaire Phases), including the PCL-5. On Day 1, all participants were asked to write about their self-identified “most traumatic event” for as long as they needed to finish their narrative (the Day 1 Writing Phase). Between Day 1 and Day 2, this narrative was read aloud by a research assistant and recorded. Participants were assigned to either the Control or Experimental Condition. For those in the Control Condition, the full audio recording was
saved as one complete file. For those in the Experimental Condition, their narrative was saved as two separate audio files (the complete file and the “prediction error” file), with the second file (i.e., the “prediction error” file) edited to abruptly halt at the “most distressing” part of the narrative. The “most distressing” part was defined as the section containing the highest density of emotion and self-referential words, as identified by the LIWC language analysis software.

On Day 2, all participants were connected to heart rate (HR) and skin conductance response (SC) recording equipment and asked to sit quietly for the Day 2 Habituation Phase (about 10 minutes, although participants were required to sit until habituation was evident in the data). Following habituation, all participants continued to sit quietly for about 5 minutes while baseline psychophysiological data were recorded (the Day 2 Baseline Phase). Once baseline data were collected, participants completed the Day 2 Activation Phase, the only phase that was different between conditions. For the Control Condition, participants listened to the full recording of their narrative a single time. For the Experimental Condition, participants listened to the “prediction error” recording a single time. All participants then played Tetris for about 25 minutes (the Day 2 Distraction Phase), followed by repeated, uninterrupted exposure to their full audio narrative until their SUDS ratings decreased by half from the Day 2 Activation Phase, or 30 minutes had passed (the Day 2 Extinction Phase). Finally, on Day 3 all participants completed another Habituation Phase, Baseline Phase, and Activation Phase (using the full audio narrative for all participants).
Amended Data Analysis Plan

Conditions

An overview of condition nomenclature can be found in Table 2. Traditionally, studies using a single case design use a standard form of notation to identify the tasks or phases (i.e., conditions) used in a study, as well as any repetitions or changes to those conditions (Gast & Spriggs, 2009). Baseline conditions are labeled A, intervention conditions labeled B, and any additional interventions are labeled C, etc. A subscript indicates an exact repetition of a previous condition (e.g., the label A\textsubscript{2} indicates the second baseline condition). A denotation of “prime” indicates an augmented repetition of a previous condition (e.g., the label A’ indicates a repetition of the baseline condition, with some change in procedure from the original baseline condition). Additionally, for the current study, a denotation of “approximation” (e.g., ~A) indicates a condition that only partially fulfills the requirements for a single-case design, but is being tentatively used for the purposes of this dissertation (e.g., the label ~A indicates a baseline condition that does not fully meet the requirements of a traditional baseline condition). Note that this later notation was created for the current study and is only used during analyses and discussion of results regarding SUDS and PCL-5 data. All described notation was used as appropriate throughout analyses and discussion of the data for the current study; specifics of its use are outlined as follows.

For both HR and SC, data collected during the Day 2 Baseline Phase represent the baseline (A\textsubscript{1}), and as such were used to approximate the stability envelopes. Data collected during the Day 2 Activation Phase represent the first intervention (B). For HR and SC data, the Day 2 Extinction Phase is unlike the Baseline Phases (i.e., there is active exposure to traumatic
Table 2
Case Series Nomenclature and Associated Descriptions by Phase

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description for Case Series Analyses</th>
<th>Nomenclature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin Conductance (SC) and Heart Rate (HR) Data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Day 1 Writing Phase</strong></td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Day 2 Baseline Phase</td>
<td>First presentation of baseline conditions</td>
<td>A₁</td>
</tr>
<tr>
<td>Day 2 Activation Phase</td>
<td>First presentation of the first intervention</td>
<td>B</td>
</tr>
<tr>
<td>Day 2 Extinction Phase</td>
<td>Presentation of the second intervention</td>
<td>C</td>
</tr>
<tr>
<td>Day 3 Baseline Phase</td>
<td>Second presentation of baseline conditions</td>
<td>A₂</td>
</tr>
<tr>
<td>Day 3 Activation Phase</td>
<td>Augmented second presentation of the first intervention</td>
<td>B’</td>
</tr>
<tr>
<td><strong>Subjective Distress (SUDS)</strong></td>
<td>First presentation of pseudobaseline conditions</td>
<td>~A</td>
</tr>
<tr>
<td><strong>Day 1 Writing Phase</strong></td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Day 2 Baseline Phase</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Day 2 Activation Phase</td>
<td>First presentation of the first intervention</td>
<td>B</td>
</tr>
<tr>
<td>Day 2 Extinction Phase</td>
<td>Augmented second presentation of pseudobaseline conditions</td>
<td>~A’</td>
</tr>
<tr>
<td>Day 3 Baseline Phase</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Day 3 Activation Phase</td>
<td>Augmented second presentation of the first intervention</td>
<td>B’</td>
</tr>
</tbody>
</table>

Note: All Questionnaire Phases (Day 1, Day 2, and Day 3), Habituation Phases (Day 2 and Day 3) and Distraction Phases (Day 2 and Day 3) were left out of the above table, as data collected during these phases were not relevant to analyses using SC, HR, or SUDS data. PTSS and intrusion symptoms data were collected via the PCL-5 during all Questionnaire Phases; due to the limited nature of this data (i.e., only three observations), PCL-5 scores from all three Questionnaire Phases were included as a single ‘condition’ for all traditional case series analyses for both PTSS and intrusion symptoms (description = presentation of the intervention condition; nomenclature = B).
stimuli) and the Activation Phases (i.e., it is not the same intervention and is not compared to any other phases to test the hypotheses). As such, HR and SC data collected during the Day 2 Extinction Phase represent a second intervention (C). Data collected during the Day 3 Baseline Phase represent the second baseline (A₂). Data collected during the Day 3 Activation Phase represent the augmented second presentation of the first intervention (B'). B' is considered augmented, as the phase is different from B for the participants that were in the Experimental Condition (the prediction error activation cue was used in B; the full activation cue was used in B'), although it was not different for those that were in the Control Condition (the full activation cue was used for B and B'). The full notation for the single-case design using HR and SC data is A₁ B A₂ B'.

Since this study was not originally designed to be a case series, no baseline SUDS data were collected. To approximate the stability envelopes for SUDS data (see within-condition analyses following this section of the document for an explanation of stability envelopes) and provide a tentative basis for comparing the effect of the first intervention on subjective distress, data during the Day 1 Writing Phase was used to represent pseudobaseline subjective distress during an emotion-inducing task (~A). This data does not fully meet the requirements of a baseline condition as it was not collected temporally adjacent to the next intervention condition, (i.e., one week elapsed between this pseudobaseline and the first intervention condition). However, it can logically be expected that an intervention designed to increase emotional response would result in data parameters similar to or greater than the parameters for the Day 1 Writing Phase (~A), and tasks designed to decrease or not engage an emotional response would result in parameters less than those of the Day 1 Writing Phase (~A). SUDS data collected during the Day 2 Activation Phase represent the first intervention (B).
Although the Day 2 Extinction Phase is an active part of the intervention, data collected during this phase was not expected to differ as a result of the intervention. As such, SUDS data during this phase are a measure of subjective distress during an emotion-inducing task over a prolonged period of time, similar to SUDS data collected during the Day 1 Writing Phase (~A). Therefore, this data was used to represent an augmented second pseudobaseline (~A'). The condition is considered augmented as it used an audio exposure instead of the written exposure used in the Day 1 Writing Phase (~A); the condition is considered a pseudobaseline as it is not temporally adjacent to the next intervention phase (i.e., one week elapsed between this pseudobaseline and the second intervention condition). However, similar to expectations regarding comparisons of SUDS data during the Day 1 Writing Phase (~A) with SUDS data during the Day 2 Activation Phase (B), it can be logically expected that an intervention designed to induce an emotional response would produce data with parameters similar to or greater than those produced during the Day 2 Extinction Phase (~A'). Finally, data collected during the Day 3 Activation Phase represent the augmented second presentation of the first intervention (B').

Again, the Day 3 Activation Phase is considered an augmented version of the first intervention due to the slight variation in procedure for participants in the Experimental Condition. The full notation for the single-case design using SUDS data is ~A B ~A’ B’. All results of analyses using SUDS data will be presented in the results section of this document; however, due to the limitations of the design with regard to these indices, interpretation of these results was conducted only within the context of the results of analyses using more robust data (i.e., the psychophysiological outcome data).

PTSS was assessed only once on each day. As such, data levels and trends were examined by treating all three days as a single intervention condition (~B). The effect of the
intervention was determined by examining the preintervention change in scores (i.e., the Day 2 PCL-5 score minus the Day 1 PCL-5 score) and the postintervention change in scores (i.e., the Day 3 PCL-5 score minus the Day 2 PCL-5 score). Standard cutoffs for reliable change in scores were used to determine treatment response (i.e., change in PCL-5 score ≥ 5) and clinically meaningful change (i.e., change in PCL-5 score ≥ 10), based on the recommendations of the National Center for PTSD within the United States Department of Veterans Affairs (2018).

Preliminary Analyses

Several checks were examined for all participants prior to hypothesis testing to determine whether several aspects of the study design worked as intended. These checks were: 1) examination of subjective distress data during the Day 1 Writing Phase (~A) to ensure the writing task was sufficient to create an emotional response, as evidence of memory activation; 2) examination of Day 2 Activation Phase HR (B), SC (B), and subjective distress; (B) data to determine if activation and extinction occurred during the activation task; and 3) examination of Day 2 Extinction Phase HR (C), SC (C), and subjective distress (~A’) data to ensure extinction occurred. Notably, these checks are substantially fewer than what were originally proposed for the aggregate data analysis. The discarded checks from the original proposal were intended to control for individual differences between participants in the two conditions. Although such checks are necessary for aggregate methods, single-case designs do not control for individual differences. Rather, they are intended to explore the effect of individual differences on treatment outcomes. As such, it was considered appropriate to drop all checks controlling for individual differences from analyses.
Primary Analyses

Within-Condition Analyses

*Condition length* represents the number of observations (i.e., data points) during that condition (Gast & Spriggs, 2009). *Level stability* represents the amount of variability between the observations; traditionally, data is considered stable when at least 80% of the data are within a certain percentage range determined by the median (i.e., the *level stability envelope*). That range varies depending on the number of observations and the clustering of the data on the scale. If there are fewer than seven observations, the range is always equal to the difference between 25% above the median and 25% below the median. If there are seven or more observations, the percentage for calculating the range of the stability envelope is 10% when data are clustered on the high end of the scale, 15% when the data are clustered in the middle, and 25% when data are clustered on the low end. The stability envelope is calculated during the first baseline for any outcome (i.e., average HR, highest SC, subjective distress), and the same envelope is used for each successive condition for that participant (i.e., data stability is defined by the first baseline data). Stable data is indicative of experimental control; once data is stable, any later changes in the data can be attributed to concurrent interventions and not extraneous variables with greater certainty (Gast & Spriggs, 2009). It is therefore important to establish data stability before changing study conditions. Gast and Spriggs (2009) recommend using the last three to five observations of a condition to determine stability before moving to the next intervention condition. Therefore, in the current study, the last three to five observations were used for all baseline (A) and psychophysiological extinction (C) conditions with greater than three data
points that show data variability (i.e., greater than 20% of the data fall outside the level stability envelope) when using all data points.

*Level change* is the amount that the outcome changes within the condition (Gast & Spriggs, 2009). *Relative level change* is the difference between the median of the first half of the data and the median of the last half of the data and is the most representative measure of level change (Gast & Spriggs, 2009). As such it will be the primary measure of level change for this study. *Absolute level change* is the difference between the first observation and the last observation of a condition (Gast & Spriggs, 2009). Absolute level change is more sensitive to variability in the data and therefore a less reliable measure of level change; however, it has the benefit of requiring only three observations (relative level change requires a minimum of four observations to calculate the two medians). As such, absolute level change is only utilized when relative level change is not possible to calculate. When the level (absolute or relative) indicates that the outcome “worsens” (i.e., HR/SC/SUDS/PTSS increases) over the condition, the data are said to be deteriorating. When the level indicates that outcomes are “getting better” (e.g., HR/SC/SUDS/PTSS decreases), the data are said to be improving.

Although level change represents the amount of actual change in medians observed during or across conditions, it is also important to assess the trend of change within the data (Gast & Spriggs, 2009). The *trend direction* is the direction of the slope of the observation series and is a measure of the pattern of change across all data points in a condition. This metric represents whether the data are increasing in value over time (i.e., accelerating), decreasing in value over time (i.e., decelerating), or not changing (i.e., zero-celerating). For example, even if level change indicates a decrease in medians during a condition, observation of a concurrent stable accelerating trend direction would indicate that the condition may be resulting in increases
in the dependent variable. It is important to assess both level change and trend direction. Level change is a measure of change that is resistant to the effect of outliers, but does not necessarily reflect the overall pattern in the data; trend direction better reflects the overall pattern of the data, but is sensitive to outliers. Together, these two metrics provide a more comprehensive picture of changes in the data within and across conditions. Trend direction is most easily assessed visually using a calculated trend line. However, if data appear to have multiple paths within the trend (e.g., data appear to be deteriorating for multiple observations, then appear to be improving for multiple observations), multiple trendlines will be created using the split-middle method (Gast & Spriggs, 2009). In addition, trend stability will be assessed by overlaying the level stability envelope along the trendline (i.e., the trend stability envelope). Trend stability represents the amount the data varies from the trendline. Trend stability is also indicative of experimental control; when a trend is stable, later variations from that trend can be attributed to intervention and not extraneous variables with greater certainty. Traditionally, a trend is considered stable when 80% or more of the data fall within the trend stability envelope (Gast & Spriggs, 2009).

**Between-Condition Analyses**

To compare data across conditions, level change between conditions were calculated for temporally adjacent conditions (Gast & Spriggs, 2009). *Absolute level change between conditions* is the difference between the last observation of a condition and the first observation of the next condition. This measure is representative of abrupt change due to the second condition. *Relative level change between conditions* is the difference between the median of the last half of one condition and the median of the first half of the next condition. This measure represents the amount of observed change due to the initiation of the second condition. To
compare data across conditions, changes in trend direction, level stability, trend stability, means, medians, and ranges are also noted. Finally, effect sizes were calculated using percentage of nonoverlapping data (PND). PND is the total number of observations for a second condition that fall outside of the range of the first condition, divided by the total number of observations for the second condition, multiplied by 100. PND represents the impact of an intervention; the higher the PND the greater the impact.

The above measures are used to assess change across adjacent conditions; however, the current study also examines differences between nonadjacent conditions (e.g., the Day 2 and Day 3 Activation Phases) to determine any effect of the intervention. To do so, level change between conditions, PND, and trend direction, level stability, trend stability, means, medians, and ranges between adjacent conditions were compared across days.

Finally, although the described, more traditional analytic techniques were used for all analyses, limitations in study design and data collected limit the interpretation of results for SUDS, PTSS, and intrusion data. However, a technique first introduced by Sidman (1960) and later expanded on by Blampied (2000; 2011) allows for more robust examination of the data within the limits of the current study. The method avoids the problem of averaging across individuals, as seen in aggregate data analysis, and allows for examination of changes in data without lengthy time series or baselines. Scores are calculated for the pre- and postinterventions being compared. The scores for all individuals are all graphed together, with the preintervention scores on the x-axis and the postintervention scores on the y-axis. A center-diagonal line is drawn though the graph; above the line representing an increase in response and below the line representing a decrease in response. Where each individual falls in relation to this line indicates the direction of magnitude and change of the measured outcome from pre- to postintervention.
Although the lack of a true baseline prevents firm conclusions, this method allows for pre- to postanalysis of case series data and comparison of treatment response across individuals without violating the rules of single-case designs (Blampied, 2011).
OVERVIEW OF RESULTS AND INTERPRETATION OF PRELIMINARY ANALYSES

For the full case series results, please see Appendix B.

Control 1

Overview of Control 1 Results

**Average Heart Rate**

Data levels and trend were stable in condition A₁. An increase in average HR was observed across the condition; however, the trend direction was first accelerating then decelerating. Data levels and trend remained stable from condition A₁ to B. There was an abrupt increase in average HR at the initiation of condition B; however, the change to condition B resulted in a decreased average HR overall. Across condition B, a decrease in average HR was observed and the trend direction was decelerating. The PND for conditions A₁ to B reflects that 0% of condition B’s data fall outside the range of condition A₁, indicating that there was no impact of condition B on average HR.

Data levels and trend were stable in condition C. An increase in average HR was observed across the condition and the trend direction was accelerating.

Data levels and trend were stable in condition A₂. A decrease in average HR was observed across the condition and the trend direction was decelerating. Data levels and trend remained stable from condition A₂ to B’. There was an abrupt increase in average HR at the initiation of condition B, and the change to condition B resulted in an increased average HR
overall. Across condition B’, a decrease in average HR was observed and the trend direction was decelerating. The PND for conditions A\textsubscript{2} to B’ reflects that 0\% of condition B’\textquotesingle s data fall outside of the range of condition A\textsubscript{2}, indicating that there was no impact of condition B’ on average HR.

There were no observed differences between A\textsubscript{1} to B and A\textsubscript{2} to B’ for PND, change in level or trend stability, or change in trend direction. See Figure 2.

---

Figure 2. Control 1 average heart rate.

*Notes:* x-axis = timing of HR measurement in seconds, y-axis = beats-per-minute (BPM). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition A\textsubscript{1} demonstrated multiple paths, so trend lines were created using the split-middle method with the middle of the data represented by a vertical red line.
Highest Skin Conductance

Data levels and trend were stable in condition A$_1$. An increase in highest SC was observed across the condition and the trend direction was accelerating. Data levels and trend remained stable from condition A$_1$ to B. There was an abrupt increase in highest SC at the initiation of condition B, and the change to condition B resulted in an increased highest SC overall. Across condition B, a decrease in highest SC was observed and the trend direction was decelerating. The PND for conditions A$_1$ to B reflects that 50% of condition B's data fall outside the range of condition A$_1$. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest skin conductance.

Data levels and trend were stable in condition C. An increase in highest SC was observed across the condition and the trend direction was accelerating.

Data levels and trend were stable in condition A$_2$. An increase in highest SC was observed across the condition and the trend direction was accelerating. Data levels became variable from condition A$_2$ to B', and trend remained stable. There was an abrupt increase in highest SC at the initiation of condition B', and the change to condition B' resulted in an increased highest SC overall. Due to data variability, no conclusions can be drawn regarding data levels across condition B'; however, a decelerating trend direction was observed. The PND for conditions A$_2$ to B' reflects that 25% of condition B’’s data fall outside of the range of condition A$_2$. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest SC.

A difference in PND was observed between A$_1$ to B and A$_2$ to B’ that suggests the effect on highest SC for condition B’ was 25% less than the effect of condition B. Absolute and relative...
change between conditions and changes in data parameters indicate that highest SC increased for both A₁ to B and A₂ to B', with a larger magnitude of change for A₂ to B'. Data remained stable in A₁ to B, but became variable in A₂ to B' despite a larger decrease in range for A₂ to B'. There were no differences in change of trend stability or direction. See Figure 3.

Figure 3. Control 1 highest skin conductance.

Notes: x-axis = timing of SC measurement in seconds, y-axis = microsiemens (μS). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition A₁ demonstrated variability, therefore only the last five observations were used in analyses. Unused data is shaded grey.
Subjective Distress

Data levels and trend were stable in condition ~A. No change in subjective distress was observed across the condition; however, the trend direction was accelerating. Data levels and trend increased in variability from condition ~A to condition B. Variable data levels and trend preclude any conclusions regarding condition B. The PND for conditions ~A to B reflects that 100% of condition B’s data fall outside the range of condition ~A. Changes in data parameters suggest that the impact of condition B was to increase subjective distress, however it is also possible that this increase is an artifact of increased data level and trend variability.

Data levels and trend were variable in condition ~A’, precluding conclusions regarding condition ~A’ or changes from ~A’ to B’. Data levels and trend remained variable in condition B’, precluding conclusions regarding condition B’.

Comparing specific changes in ~A to B to changes in ~A’ to B’ is precluded by the data level and trend variability in ~A’ to B’. See Figure 4.

Posttraumatic Stress Symptoms

For total symptoms, data levels were variable, precluding conclusions regarding changes in data levels across the three days. Data trend was stable; data were decelerating. Total symptoms decreased prior to the intervention, but decreased more following the intervention.

For intrusion symptoms, data levels were variable, precluding conclusions regarding changes in data levels across the three days. Data trend was stable; data were decelerating. Intrusion symptoms decreased prior to the intervention, and decreased more following the intervention. See Figure 5.
Figure 4. Control 1 subjective distress.

*Notes:* x-axis = timing of SUDS rating, y-axis = SUDS ratings; Pre = SUDS prior to the start of the phase, Highest = highest SUDS during the phase, Post = SUDS after the phase concluded. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.

Figure 5. Control 1 total PTSS and intrusion symptoms.

*Notes:* x-axis = timing of PCL-5 administration, y-axis = PCL-5 score. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.
Interpretation of Control 1 Preliminary Analyses

For Control 1, subjective distress data were stable across the Day 1 Writing Phase (~A), and there was no relative level change. However, the trend was stable and the trend direction was accelerating, suggesting that the writing task was increasing Control 1’s subjective distress as expected.

Although the activation task on Day 2 (B) appeared to create an initial increase in HR following baseline data collection (A₁), PND suggests a 0% overall change across the condition. These results suggest that the activation task may not have resulted in the expected activation, or that the activation was more transient than expected. Examination of SC data provides more compelling evidence that the activation task was successful, as an initial and overall increase in SC was observed during the activation task (B) compared to baseline (A₁), with a PND suggesting an actual increase of 50% across the condition. The presence of this 50% increase in SC suggests that psychophysiological activation did in fact occur, despite the lack of an observed effect on average HR. The lack of effect on average HR may also be reflected in the trend analysis, as a stable decelerating trend was observed at the end of baseline (A₁) and continued through the activation task (B). However, when considered in conjunction with the stable accelerating trend for SC in the Day 2 Baseline Phase (A₁) that changed to a stable decelerating trend in the Day 2 Activation Phase (B), it seems likely that extinction occurred for Control 1 during the task, as would be expected for a control condition participant. Unfortunately, but not surprisingly, the subjective distress data and trend for Control 1 both became variable in the Day 2 Activation Phase (B); thus, this data could not be examined to determine whether extinction occurred in this phase. This increase in variability was not surprising as data collection methods
for subjective distress limited the Day 2 Activation Phase (B) to three time points, which is likely insufficient to establish data and trend stability. It is therefore appropriate to rely on the two primary outcome measures, HR and SC, to determine the presence of extinction during the activation task, and as such, it seems likely that extinction occurred during the Day 2 Activation Phase (B).

The presence of extinction during the Day 2 Extinction Phase was also examined. Surprisingly, both HR and SC data demonstrated deteriorating relative level change and a stable accelerating trend, suggesting that extinction may not have occurred during the Day 2 Extinction Phase (C), and instead, psychophysiological responding may have increased contrary to expectations. Yet again, subjective distress data level and trend were variable and unable to be interpreted. For this study, extinction was operationalized as subjective distress decreasing by half, which occurred after three time points for Control 1; thus, this increase in variability is not unexpected, although it is inconvenient. Thus, as with examination of extinction during the Day 2 Activation Phase, interpretation relies on the two primary outcome measures, which both indicate moderate increases in psychophysiological responding during the Day 2 Extinction Phase (C).

Control 2

Overview of Control 2 Results

Average Heart Rate

Data levels and trend were stable in condition A1. A decrease in average heart rate was observed across the condition and the trend direction was decelerating. Data levels and trend
remained stable from condition A₁ to B. There was an abrupt decrease in average HR at the
initiation of condition B, and the change to condition B resulted in a decrease in average HR
overall. Across condition B, a decrease in average heart rate was observed, and the trend
direction was decelerating. The PND for conditions A₁ to B reflects that 90% of condition B's
data fall outside the range of condition A₁. Examination of level change between conditions and
changes in data parameters suggests that the impact of condition B was to decrease HR.

Data levels and trend were stable in condition C. An increase in average HR was
observed across the condition, and the trend direction was accelerating.

Data levels and trend were stable in condition A₂. A decrease in average HR was
observed across the condition, and the trend direction was decelerating. Data levels and trend
remained stable from condition A₂ to B’. There was an abrupt increase in average HR at the
initiation of condition B’, and the change to condition B’ resulted in an increased HR overall.
Across condition B’, a decrease in average HR was observed, and the trend direction was
decelerating. The PND for conditions A₂ to B’ reflects that 100% of condition B’’s data fall
outside of the range of condition A₂. Examination of level change between conditions and
changes in data parameters suggests that the impact of condition B’ was to increase HR.

A difference in PND was observed that suggests the impact of condition B’ on average
heart rate was 10% greater in A₂ to B’. Absolute and relative change between conditions and
change in means indicate that average HR decreased for A₁ to B and increased for A₂ to B’,
although medians increased in both. The magnitude of change was larger for abrupt change in A₂
to B’ but smaller for change overall. There were no differences in change of level or trend
stability, or trend direction. See Figure 6.
Figure 6. Control 2 average heart rate.

Notes: x-axis = timing of HR measurement in seconds, y-axis = beats-per-minute (BPM). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.

**Highest Skin Conductance**

Data levels and trend were stable in condition A₁. An increase in highest SC was observed across the condition, and the trend direction was accelerating. Data levels and trend remained stable from condition A₁ to B. There was an abrupt decrease in highest SC at the
initiation of condition B; however, the change to condition B resulted in an increase in highest SC overall. Across condition B, an increase in highest SC was observed and the trend direction was accelerating. The PND for conditions A\textsubscript{1} to B reflects that 10\% of condition B’s data fall outside the range of condition A\textsubscript{1}. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest SC, despite an initial decrease.

Data levels and trend were stable in condition C. An increase in highest SC was observed across the condition, and the trend direction was accelerating.

Data levels and trend were stable in condition A\textsubscript{2}. An increase in highest SC was observed across the condition, and the trend direction was accelerating. Data levels and trend remained stable from condition A\textsubscript{2} to B’. There was an abrupt increase in highest SC at the initiation of condition B’, and the change to condition B’ resulted in an increase in highest SC overall. Across condition B’, a decrease in highest SC was observed, and the trend direction was decelerating. The PND for conditions A\textsubscript{2} to B’ reflects that 89\% of condition B’’s data fall outside of the range of condition A\textsubscript{2}. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest SC.

A difference in PND was observed that suggests the effect of condition B’ on highest SC was 79\% greater than the effect of condition B. Absolute level change between conditions indicated an abrupt decrease in highest SC for A\textsubscript{1} to B and an abrupt increase for A\textsubscript{2} to B’; relative level change between conditions and changes in data parameters indicate that highest SC increased for both A\textsubscript{1} to B and A\textsubscript{2} to B’. The magnitude of change was larger for abrupt change in A\textsubscript{2} to B’, but smaller for change overall. There were no differences in change of level or trend stability. Trend direction remained accelerating in A\textsubscript{1} to B, but changed from accelerating to decelerating in A\textsubscript{2} to B’. See Figure 7.
Subjective Distress

Data levels and trend were stable in condition ~A. No change in subjective distress was observed across the condition; however, the trend direction was accelerating. Data levels and trend increased in variability from condition ~A to condition B. Variable data levels and trend preclude any conclusions regarding condition B. The PND for conditions ~A to B reflects that...
100% of condition B’s data fall outside the range of condition ~A. Changes in data parameters suggest that the impact of condition B was to increase subjective distress; however, it is also possible that this increase is an artifact of increased data level and trend variability.

Data levels and trend were stable in condition ~A’. An increase in subjective distress was observed across the condition, and the trend was accelerating. Data levels and trend remained stable in condition B’. Across condition B’, an increase in subjective distress was observed, and the trend was accelerating. The PND for conditions ~A’ to B’ reflects that 33% of condition B’’s data fall outside of the range of condition ~A’. Changes in data parameters suggest that the impact of condition B’ was to decrease subjective distress.

A difference in PND was observed between ~A to B and ~A’ to B’ that suggests the effect on subjective distress for condition B’ was 67% less than effect of condition B. Changes in data parameters indicate that subjective distress increased for ~A to B, and decreased for ~A’ to B’, with a larger magnitude of change for ~A’ to B’. Data and trend became variable in ~A to B, but remained stable in ~A’ to B’. Differences in change of trend direction could not be examined, due to trend variability in condition B. See Figure 8.

Posttraumatic Stress Symptoms

For total symptoms, data levels and trend were stable. Total PTSS decreased across the three days and the trend direction was decelerating. Total symptoms decreased prior to the intervention but decreased more following the intervention. For intrusion symptoms, data levels and trend were variable, precluding conclusions regarding changes in data levels or trend direction across the three days. Intrusion symptoms increased prior to the intervention but decreased following the intervention. See Figure 9.
Figure 8. Control 2 subjective distress.

*Notes:* x-axis = timing of SUDS rating, y-axis = SUDS ratings; Pre = SUDS prior to the start of the phase, Highest = highest SUDS during the phase, Post = SUDS after the phase concluded. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition A demonstrated variability, therefore only the last five observations were used in analyses. Unused data is shaded grey.

Figure 9. Control 2 total PTSS and intrusion symptoms.

*Notes:* x-axis = timing of PCL-5 administration, y-axis = PCL-5 intrusion subscale score. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.
Interpretation of Control 2 Preliminary Analyses

As with Control 1, Control 2’s subjective distress data were stable across the Day 1 Writing Phase (~A) and there was no relative level change, yet a stable accelerating trend suggests that the writing task was increasing Control 2’s subjective distress as expected.

Unlike Control 1, the activation task on Day 2 (B) appeared to create an initial and overall decrease in HR following baseline data collection (A₁) with PND suggesting a 90% actual decrease across the condition. Similar to Control 1, a stable decelerating trend was observed during the Day 2 Baseline Phase (A₁) and continued through the Day 2 Activation Phase (B). These results suggest that the activation task may not have resulted in the expected activation. Examination of SC data does provide some evidence that the activation task was successful in increasing activation, as an overall increase in SC was observed with PND suggesting a 10% actual increase. However, the SC at the onset of the Day 2 Activation Phase (B) surprisingly decreased. Trend analysis revealed a stable accelerating trend during baseline (A₁) that remained accelerating during activation (B). Taken together, Control 2’s HR data suggests nonreactivity (similar to the HR data for Control 1), while Control 2’s SC data suggests that extinction did not occur, contrary to expectations for a control condition participant. As with Control 1, the subjective distress data and trend for Control 2 both became variable in the Day 2 Activation Phase (B), thus this data could not be examined to determine whether extinction occurred in this phase. Again, relying on the two primary outcome measures, HR and SC, to determine the presence of extinction during the activation task, it seems likely that extinction did not occur, and it is possible that the activation task was not sufficient to induce psychophysiological reactivity.
The presence of extinction during the Day 2 Extinction Phase was also examined. Surprisingly and similar to Control 1, both HR and SC data demonstrated deteriorating relative level change and a stable accelerating trend, suggesting that extinction may not have occurred during the Day 2 Extinction Phase (C), and instead psychophysiological responding may have increased contrary to expectations. Unlike Control 1, sufficient subjective distress data was collected to establish level and trend stability for Control 2. As with HR and SC, subjective distress data demonstrated deterioration and a stable accelerating trend. Altogether, HR, SC, and subjective distress data all suggest it is likely that extinction did not occur during the Day 2 Extinction Phase, and instead psychophysiological responding and subjective distress increased contrary to expectations.

Intervention 1

Overview of Intervention 1 Results

Average Heart Rate

Data levels and trend were stable in condition A₁. A decrease in average HR was observed across the condition, and the trend direction was decelerating. Data levels and trend remained stable from condition A₁ to B. There was an abrupt increase in average HR at the initiation of condition B, and the change to condition B resulted in an increase in average HR overall. Across condition B, a decrease in average HR was observed, and the trend direction was decelerating. The PND for conditions A₁ to B reflects that 100% of condition B’s data fall outside the range of condition A₁. Examination of level change between conditions and changes in data parameters suggest that the impact of condition B was to increase HR.
Data levels and trend were stable in condition C. A decrease in average HR was observed across the condition, and the trend direction was decelerating.

Data levels and trend were stable in condition A. A decrease in average HR was observed across the condition and the trend direction was decelerating. Data levels and trend remained stable from condition A to B. There was an abrupt increase in average HR at the initiation of condition B, and the change to condition B resulted in an increase in average HR overall. Across condition B, a decrease in average HR was observed, and the trend direction was decelerating-accelerating. The PND for conditions A to B reflects that 36% of condition B’s data fall outside of the range of condition A. Examination of level change between conditions and changes in data parameters suggest that the impact of condition B was to increase HR.

A difference in PND was observed between A to B and A to B’ that suggests the effect of condition B’ on average HR was 64% less than the effect of condition B. Absolute and relative change between conditions and changes in data parameters indicate that average HR increased for both A to B and A to B’. The magnitude of change was larger for abrupt change in A to B’, but smaller for change overall. There were no differences in changes of level or trend stability, or trend direction. See Figure 10.

**Highest Skin Conductance**

Data levels and trend were stable in condition A. An increase in highest SC was observed across the condition and the trend direction was accelerating-decelerating. Data levels and trend remained stable from condition A to B. There was an abrupt increase in highest SC at the initiation of condition B, and condition B resulted in an increase in highest SC overall. Across condition B, an increase in highest SC was observed and the trend direction was
Figure 10. Intervention 1 average heart rate.

Notes: x-axis = timing of HR measurement in seconds, y-axis = beats-per-minute (BPM). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition B' demonstrated multiple paths, so trend lines were created using the split-middle method with the middle of the data represented by a vertical red line.
accelerating-decelerating. The PND for conditions A₁ to B reflects that 100% of condition B’s data fall outside the range of condition A₁. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest SC.

Data levels and trend were stable in condition C. An increase in highest SC was observed across the condition and the trend direction was accelerating.

Data levels and trend were stable in condition A₂. An increase in highest SC was observed across the condition, and the trend direction was decelerating. Data levels remained stable from condition A₂ to B’. There was an abrupt increase in highest SC at the initiation of condition B’, and the change to condition B’ resulted in an increase in highest SC overall. Across condition B’, an increase in highest SC was observed and the trend direction was decelerating-accelerating. The PND for conditions A₂ to B’ reflects that 82% of condition B’s data fall outside of the range of condition A₂. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest skin conductance.

A difference in PND was observed between A₁ to B and A₂ to B’ that suggests the effect of condition B’ on highest SC was 18% less than the effect of condition B on highest SC. Absolute and relative change between conditions and changes in data parameters indicate that highest SC increased for both A₁ to B and A₂ to B’, with a smaller magnitude of change for A₂ to B’. There were no differences in changes of level or trend stability. Trend direction changed from decelerating to accelerating in A₁ to B, and remained decelerating in A₂ to B’. See Figure 11.
Figure 11. Intervention 1 highest skin conductance.

Notes: x-axis = timing of SC measurement in seconds, y-axis = microsiemens (μS). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for conditions A₁, B, and B’ demonstrated multiple paths, so trend lines were created using the split-middle method with the middle of the data represented by a vertical red line.
Subjective Distress

Data levels and trend were variable in condition ~A, precluding any conclusions regarding condition ~A or changes from condition ~A to condition B. Data levels and trend remained variable in condition B, precluding any conclusions regarding condition B.

Data levels and trend were variable in condition ~A’, precluding any conclusions regarding condition ~A’ or changes from condition ~A’ to condition B’. Data levels and trend remained variable in condition B’, precluding any conclusions regarding condition B’.

Data variability in all conditions precludes conclusions drawn from the available subjective distress data. See Figure 12.

Figure 12. Intervention 1 subjective distress.

Notes: x-axis = timing of SUDS rating, y-axis = SUDS ratings; Pre = SUDS prior to the start of the phase, Highest = highest SUDS during the phase, Post = SUDS after the phase concluded. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.
Posttraumatic Stress Symptoms

For total symptoms, data levels and trend were variable, precluding conclusions regarding changes in data levels or trend direction across the three days. Total symptoms decreased prior to the intervention and did not change following the intervention.

For intrusion symptoms, data levels were variable, precluding conclusions regarding changes in data levels across the three days. However, trend was stable; intrusion symptoms were decelerating across the three days. Intrusion symptoms decreased prior to the intervention and decreased less following the intervention. See Figure 13.

Figure 13. Intervention 1 total PTSS and intrusion symptoms.

Notes: x-axis = timing of PCL-5 administration, y-axis = PCL-5 intrusion subscale score. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.

Interpretation of Intervention 1 Preliminary Analyses

Intervention 1’s subjective distress data were variable across the Day 1 Writing Phase (~A). As such, no conclusions could be drawn regarding the effectiveness of the writing task to produce a narrative sufficient to induce activation.
Unlike both control condition participants, the activation task on Day 2 (B) appeared to create an initial and overall increase in HR following baseline data collection (A), with PND suggesting a 100% actual increase across the condition. A stable decelerating trend was observed during the Day 2 Baseline Phase (A) and continued through the Day 2 Activation Phase (B). These results suggest that the activation task did result in the expected activation; however, extinction may have occurred during the activation task contrary to expectations for an intervention condition participant. Examination of SC data corroborates these findings. An initial and overall increase in SC was observed during the activation task (B), with PND suggesting a 100% actual increase. A stable decelerating trend was observed at the end of baseline (A), and although a stable accelerating trend was observed early in the activation phase (B), a stable decelerating trend had developed by the end of that phase. As with both control condition participants, data level and trend variability preclude examination of extinction of subjective distress during the Day 2 Activation Phase (B). Yet the two primary outcome measures clearly suggest that the activation task was successful, but that extinction likely occurred prior to the end of the task, contrary to expectations.

The presence of extinction during the Day 2 Extinction Phase was also examined. Unlike the control condition participants, results were mixed. Where HR data demonstrated improvement and a stable decelerating trend, SC data deteriorated and demonstrated a stable accelerating trend. Variability of data level and trend prevent interpretation of the subjective distress data during this phase (~A'). While the HR and SC results are mixed, precluding firm conclusions, the HR data may imply that some amount of extinction did occur, as expected.
Intervention 2

Overview of Intervention 2 Results

Average Heart Rate

Data levels and trend were stable in condition A₁. An increase in average HR was observed across the condition, and the trend direction was accelerating. Data levels and trend remained stable from condition A₁ to B. There was an abrupt decrease in average HR at the initiation of condition B; however, the change to condition B resulted in an increase in average HR overall. Across condition B, a decrease in average HR was observed, and the trend direction was accelerating-decelerating. The PND for conditions A₁ to B reflects that 67% of condition B’s data fall outside the range of condition A₁. Examination of level change across conditions and changes in data parameters suggests that the impact of condition B was to increase HR, despite an initial decrease.

Data levels and trend were stable in condition C. An increase in average HR was observed across the condition, and the trend direction was accelerating.

Data levels and trend were stable in condition A₂. An increase in average HR was observed across the condition and the trend direction was accelerating. Data levels and trend remained stable from condition A₂ to B’. There was an abrupt increase in average HR at the initiation of condition B’, and the change to condition B’ resulted in an increase in average HR overall. Across condition B’, a decrease in average HR was observed, and the trend direction was decelerating. The PND for conditions A₂ to B’ reflects that 100% of condition B’’s data fall
outside of the range of condition A\textsubscript{2}. Examination of level change across conditions and changes in data parameters suggest that the impact of condition B' was to increase average HR.

A difference in PND was observed between A\textsubscript{1} to B and A\textsubscript{2} to B' that suggests the effect of condition B' on average HR was 33\% greater than the effect of condition B. Absolute level change between conditions indicated an abrupt decrease in average HR for A\textsubscript{1} to B and an abrupt increase for A\textsubscript{2} to B'; relative level change between conditions and changes in data parameters indicate that average HR increased for both A\textsubscript{1} to B and A\textsubscript{2} to B'. The magnitude of change was larger for abrupt change in A\textsubscript{2} to B' but generally smaller for change overall, although the magnitude of change in means was larger. There were no differences in change of level or trend stability. Trend direction remained accelerating in A\textsubscript{1} to B, and changed from accelerating to decelerating in A\textsubscript{2} to B'. See Figure 14.

**Highest Skin Conductance**

Data levels and trend were stable in condition A\textsubscript{1}. An increase in highest SC was observed across the condition and the trend direction was accelerating. Data levels and trend remained stable from condition A\textsubscript{1} to B. There was an abrupt decrease in highest SC at the initiation of condition B, and the change to condition B resulted in an increased in highest SC overall. Across condition B, a decrease in highest SC was observed and the trend direction was decelerating. The PND for conditions A\textsubscript{1} to B reflects that 33\% of condition B's data fall outside the range of condition A\textsubscript{1}. Examination of level change between conditions and changes in data parameters suggests that this impact was to decrease highest SC.
Figure 14. Intervention 2 average heart rate.

*Notes:* x-axis = timing of HR measurement in seconds, y-axis = beats-per-minute (BPM). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition B demonstrated multiple paths, so trend lines were created using the split-middle method with the middle of the data represented by a vertical red line.
Data levels and trend were stable in condition C. A decrease in highest SC was observed across the condition, and the trend direction was decelerating.

Data levels and trend were stable in condition A₂. An increase in highest SC was observed across the condition, and the trend direction was accelerating-decelerating. Data levels remained stable from condition A₂ to B’. There was an abrupt increase in highest SC at the initiation of condition B’, however, the change to condition B’ resulted in a decrease in highest SC overall. Across condition B’, a decrease in highest SC was observed and the trend direction was decelerating. The PND for conditions A₂ to B’ reflects that 20% of condition B’’s data fall outside of the range of condition A₂. Examination of level change between conditions and changes in data parameters suggests that this impact was to decrease highest SC, despite an initial increase.

A difference in PND was observed between A₁ to B and A₂ to B’ that suggests the effect of condition B’ on highest SC was 13% less than the effect of condition B. Absolute level change between conditions indicated an abrupt decrease in highest SC for A₁ to B and an abrupt increase for A₂ to B’; relative level change between conditions and changes in data parameters indicate that highest SC decreased for both A₁ to B and A₂ to B’. The magnitude of change was larger for A₂ to B’ although the magnitude of change in medians was smaller for A₂ to B’. There were no differences in change of level or trend stability. Trend direction changed from accelerating to decelerating in A₁ to B, and remained decelerating in A₂ to B’. See Figure 15.

Subjective Distress

Data levels and trend were stable in condition ~A. A decrease in subjective distress was observed across the condition and the trend direction was decelerating. Data levels and trend
Figure 15. Intervention 2 highest skin conductance.

*Notes:* x-axis = timing of SC measurement in seconds, y-axis = microsiemens (μS). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for conditions A2 and C demonstrated variability, therefore only the last five observations were used in analyses. Unused data is shaded grey. Data for condition A2 demonstrated multiple paths, so trend lines were created using the split-middle method with the middle of the data represented by a vertical red line.
remained stable in condition B. Across condition B, an increase in subjective distress was observed and the trend direction was accelerating. The PND for conditions ~A to B reflect that 100% of condition B’s data fall outside of the range of condition A. Examination of changes in data parameters between the two conditions suggests that the effect of condition B was to decrease subjective distress.

Data levels were stable in condition ~A’. A decrease in subjective distress was observed across the condition. Trend was variable precluding any conclusions about trend direction during condition ~A’ or changes in trend direction between ~A’ and B’. Data levels became variable, and trend remained variable in condition B’ precluding conclusions regrading condition B’. The PND for conditions ~A’ to B’ reflect that 0% of condition B’’s data fall outside of the range of condition ~A’, suggesting that the only effect of condition B’ was to increase data variability.

A difference in PND was observed between ~A to B and ~A’ to B’ that suggests the effect on subjective distress for condition B’ was 100% less than effect of condition B. Changes in data parameters indicate that subjective distress decreased for both ~A to B and ~A’ to B’ with a smaller magnitude of change in means for ~A’ to B’ and no difference in magnitude of change in medians. However, observed changes in data parameters for ~A’ to B’ may be due to the increase in data variability in B’. Data remained stable in ~A to B and became variable in ~A’ to B’; there was no difference in change of trend stability. Differences in change of trend direction could not be examined, due to trend variability in ~A’ to B’. See Figure 16.
Figure 16. Intervention 2 subjective distress.

*Notes:* x-axis = timing of SUDS rating, y-axis = SUDS ratings; Pre = SUDS prior to the start of the phase, Highest = highest SUDS during the phase, Post = SUDS after the phase concluded. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition A demonstrated variability, therefore only the last five observations were used in analyses. Unused data is shaded grey.

**Posttraumatic Stress Symptoms**

For total symptoms, data levels and trend were stable. A decrease in total PTSS was observed across the three days, and the trend direction was decelerating. Total symptoms decreased prior to the intervention and decreased less following the intervention.

For intrusion symptoms, data levels were variable, precluding conclusions regarding changes in data levels across the three days. However, trend was stable; intrusion symptoms were decelerating across the three days. Intrusion symptoms decreased prior to the intervention and did not change following the intervention. See Figure 17.
Figure 17. Intervention 2 total PTSS and intrusion symptoms.

Notes: x-axis = timing of PCL-5 administration, y-axis = PCL-5 intrusion subscale score. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.

Interpretation of Intervention 2 Preliminary Analyses

Unlike the control condition participants and Intervention 1, Intervention 2’s subjective distress data demonstrated improvement and a stable decelerating trend across the Day 1 Writing Phase (~A). It is therefore possible that the writing task was not sufficient to create an activating narrative for Intervention 2.

Unlike both control condition participants and Intervention 1, the activation task on Day 2 (B) appeared to create an initial decrease but overall increase in HR following baseline data collection (A₁), with PND suggesting a 67% actual increase across the condition. A stable accelerating trend was observed during the Day 2 Baseline Phase (A₁) and continued into the Day 2 Activation Phase (B); however, this trend changed to a stable decelerating trend by the end of the phase. These results suggest that the activation task did result in the expected activation; however, extinction may have occurred during the activation task (B) contrary to expectations for an intervention condition participant. As with HR, an initial decrease but overall increase in SC was observed during the activation task (B). However, unlike Intervention 2’s HR
data, PND for SC suggested a 33% actual decrease. A stable accelerating trend was observed during baseline \( (A_1) \), which changed to a stable decelerating trend during activation. Unlike the HR data, Intervention 2’s SC data may suggest an unsuccessful activation task as well as unexpected extinction during this phase \( (B) \). Unlike both control condition participants and Intervention 1, subjective distress data level and trend were stable during the Day 2 Activation Phase \( (B) \). An increase in subjective distress was observed, but PND suggests a 100% actual decrease, despite a stable accelerating trend. Taken together, HR data suggests that the activation task may have resulted in some activation, although SC and subjective distress data shed doubt on this interpretation. If activation did in fact occur, the data indicates that extinction was also likely during this phase, contrary to expectations.

The presence of extinction during the Day 2 Extinction Phase was also examined. Similar to Intervention 1, results were mixed, although they were mixed in a different way. Unlike Intervention 1, HR data demonstrated deterioration and a stable accelerating trend, and SC data demonstrated improvement and a stable decelerating trend. Also unlike Intervention 1, and indeed unlike the control condition participants as well, Intervention 2’s subjective distress data were interpretable for the Day 2 Extinction Phase \( (~A’) \). A decrease in subjective distress was observed with a stable decelerating trend. Despite the results of Intervention 2’s HR data, Intervention 2’s SC and subjective distress data both suggest that some amount of extinction did in fact occur.
Intervention 3

Overview of Intervention 3 Results

Average Heart Rate

Data levels and trend were stable in condition $A_1$. A decrease in average HR was observed across the condition, and the trend direction was decelerating. Data levels and trend remained stable from condition $A_1$ to $B$. There was an abrupt decrease in average HR at the initiation of condition $B$; however, the change to condition $B$ resulted in an increase in average HR overall. Across condition $B$, an increase in average HR was observed, and the trend direction was accelerating. The PND for conditions $A_1$ to $B$ reflects that 0% of condition $B$'s data fall outside the range of condition $A_1$, suggesting no effect of condition $B$ on average HR.

Data levels and trend were stable in condition $C$. An increase in average HR was observed across the condition, and the trend direction was accelerating.

Data levels and trend were stable in condition $A_2$. An increase in average HR was observed across the condition, and the trend direction was accelerating. Data levels and trend remained stable from condition $A_2$ to $B'$. There was an abrupt decrease in average HR at the initiation of condition $B'$, and the change to condition $B'$ resulted in a decrease in average HR overall. Across condition $B'$, an increase in average HR was observed, and the trend direction was decelerating. The PND for conditions $A_2$ to $B'$ reflects that 0% of condition $B'$'s data fall outside of the range of condition $A_2$, suggesting that there was no effect of condition $B'$ on average HR.
There were no observed differences between \( A_1 \) to \( B \) and \( A_2 \) to \( B' \) for PND or change in level or trend stability. Trend direction changed from decelerating to accelerating in \( A_1 \) to \( B \), and from accelerating to decelerating in \( A_2 \) to \( B' \). See Figure 18.

Figure 18. Intervention 3 average heart rate.

*Notes:* \( x \)-axis = timing of HR measurement in seconds, \( y \)-axis = beats-per-minute (BPM). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.
Highest Skin Conductance

Data levels and trend were stable in condition A1. An increase in highest SC was observed across the condition, and the trend direction was decelerating-accelerating. Data levels and trend remained stable from condition A1 to B. There was an abrupt decrease in highest SC at the initiation of condition B; however, the change to condition B resulted in an increase in highest SC overall. Across condition B, a decrease in highest SC was observed, and the trend direction was decelerating. The PND for conditions A1 to B reflects that 60% of condition B's data fall outside the range of condition A1. Examination of level change between conditions and changes in data parameters suggests that this impact was to increase highest SC despite an initial decrease.

Data levels and trend were stable in condition C. A decrease in highest SC was observed across the condition, and the trend direction was decelerating.

Data levels and trend were stable in condition A2. A decrease in highest SC was observed across the condition, and the trend direction was decelerating. Data levels remained stable from condition A2 to B'. There was an abrupt decrease in highest SC at the initiation of condition B', and the change to condition B' resulted in a decrease in highest SC overall. Across condition B', an increase in highest SC was observed, and the trend direction was decelerating. The PND for conditions A2 to B' reflects that 0% of condition B's data fall outside of the range of condition A2 suggesting that there was no effect of condition B'.

A difference in PND was observed between A1 to B and A2 to B' that suggests the effect of condition B' on highest SC was 60% less than the effect of condition B. Absolute level change between conditions indicated an abrupt decrease in highest SC for both A1 to B and A2 to B’;
relative level change between conditions indicated that highest SC increased for \(A_1\) to \(B\) and decreased from \(A_2\) to \(B'\). However, changes in data parameters indicated that highest SC increased for both. The magnitude of change was larger for abrupt change in \(A_2\) to \(B'\), but smaller for change overall. There were no differences in change of level or trend stability. Trend direction changed from accelerating to decelerating in \(A_1\) to \(B\) and remained decelerating in \(A_2\) to \(B'\). See Figure 19.

**Subjective Distress**

Data levels and trend were stable in condition \(~A\). An increase in subjective distress was observed across the condition, and the trend direction was accelerating. Data levels became variable in condition \(B\), precluding conclusions regrading condition \(B'\). However, the trend direction remained stable; data in condition \(B\) were accelerating. The PND for conditions \(~A\) to \(B\) reflect that 100% of condition \(B'\)'s data fall outside of the range of condition \(~A\). Changes in data parameters suggest that the effect of condition \(B\) was to increase subjective distress.

Data levels and trend were stable in condition \(~A'\). An increase in subjective distress was observed across the condition, and the trend direction was accelerating. Data levels became variable in condition \(B'\), precluding conclusions regarding condition \(B'\). However, the trend direction remained stable; data in condition \(B'\) were accelerating. The PND for conditions \(~A'\) to \(B'\) reflect that 33% of condition \(B'\)'s data fall outside of the range of condition \(~A'\). Changes in data parameters suggest that the effect of condition \(B'\) was to decrease subjective distress.

A difference in PND was observed between \(~A\) to \(B\) and \(~A'\) to \(B'\) that suggests the effect on subjective distress for condition \(B'\) was 67% less than the effect of condition \(B\). Changes in data parameters indicate that subjective distress increased for \(~A\) to \(B\), and decreased
Figure 19. Intervention 3 highest skin conductance.

Notes: x-axis = timing of SC measurement in seconds, y-axis = microsiemens (μS). The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition A1 demonstrated multiple paths, so trend lines were created using the split-middle method with the middle of the data represented by a vertical red line. Data for condition A2 demonstrated variability, therefore only the last five observations were used in analyses. Unused data is shaded grey.
for ~A’ to B’, with a larger magnitude of change in mean, but smaller magnitude of change in median, for ~A’ to B’. There were no differences in change of level or trend stability, or trend direction. See Figure 20.

![Graph A](image)

![Graph B](image)

![Graph A’](image)

![Graph B’](image)

**Figure 20.** Intervention 3 subjective distress.

*Notes:* x-axis = timing of SUDS rating, y-axis = SUDS ratings; Pre = SUDS prior to the start of the phase, Highest = highest SUDS during the phase, Post = SUDS after the phase concluded. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line. Data for condition A demonstrated variability, therefore only the last five observations were used in analyses. Unused data is shaded grey.

**Posttraumatic Stress Symptoms**

For total symptoms, data levels and trend were stable. A decrease in total PTSS was observed across the three days, and the trend direction was decelerating. Total symptoms decreased prior to the intervention and decreased less following the intervention.
For intrusion symptoms, data levels were variable, precluding conclusions regarding changes in data levels across the three days. However, trend was stable; intrusion symptoms were decelerating across the three days. Intrusion symptoms did not change prior to the intervention but decreased following the intervention. See Figure 21.

![Figure 21. Intervention 3 total PTSS and intrusion symptoms.](image)

*Notes: x-axis = timing of PCL-5 administration, y-axis = PCL-5 intrusion subscale score. The median is represented by the solid blue line; the trend is represented by the solid black line; the level stability envelope is represented by the dotted blue line; the trend stability envelope is represented by the dotted black line.*

**Interpretation of Intervention 3 Preliminary Analyses**

Although data levels for Intervention 3’s subjective distress during the Day 1 Writing Phase (~A) were variable, a stable accelerating trend was observed. This trend suggests that, similar to the control condition participants, the writing task may have been sufficient to create a narrative that induced activation.

For Intervention 3, the activation task on Day 2 (B) appeared to create an initial decrease but overall increase in HR following baseline data collection (A1). However, like Control 1, Intervention 3’s PND suggested a 0% actual change across the condition (B). Unlike Control 1, a change in trend direction was observed from decelerating in baseline (A1) to accelerating during
activation (B), which may indicate a lack of extinction during Intervention 3’s activation phase (B). Yet, the PND of 0% seems to indicate a lack of effect of the activation task on HR.

Intervention 3’s SC data also demonstrated an initial decrease and overall increase. Unlike their HR data, Intervention 3’s SC PND suggested a 60% actual increase, suggesting the activation task did result in activation. However, SC trend direction changed from a stable accelerating trend at the end of baseline (A) to a stable decelerating trend during activation (B) suggesting extinction likely occurred. Intervention 3’s Day 2 Activation Phase (B) subjective distress data levels were variable; however, a stable accelerating trend was observed suggesting extinction did not occur. PND suggested a 100% increase in subjective distress due to the activation task, providing some further support for the lack of extinction; however, the variability in data levels precludes firm conclusions. Therefore, Intervention 3’s HR, SC, and subjective distress data are mixed at best. It is likely that the activation task was sufficient to induce activation, but the presence of extinction in the SC data indicated that some amount of extinction may have occurred, contrary to expectations.

The presence of extinction during the Day 2 Extinction Phase was also examined. Intervention 3’s results were mixed and similar to those of Intervention 2. HR data demonstrated deterioration and a stable accelerating trend and SC data demonstrated improvement and a stable decelerating trend. Also similar to Intervention 2, Intervention 3’s subjective distress data were interpretable for the Day 2 Extinction Phase (~A’). Unlike Intervention 2, an increase in subjective distress was observed with a stable accelerating trend. Despite the results of Intervention 3’s HR and subjective distress data, Intervention 3’s SC data suggests that some amount of extinction did in fact occur.
Blampied (2011) Technique

Due to limitations in study design and/or data collected, the results described above for the subjective distress, PTSS, and intrusion data are limited. Therefore, these measures were also analyzed and compared across participants using the technique described by Blampied (2011).

**Subjective Distress**

The difference in self-reported subjective distress scores from pre-Day 2 Activation Phase to highest during the Day 2 Activation Phase were calculated for all participants and graphed along the x-axis of Figure 22. The difference in self-reported subjective distress scores from pre-Day 3 Activation Phase to highest during the Day 3 Activation Phase were also calculated for all participants and graphed along the y-axis of the same figure. A line representing no change from pre- to postintervention was drawn from (0, 0) to (100, 100). Results for Control 1, Control 2, and Intervention 1 indicated decreases in subjective distress from pre- to postintervention (10 units, 55 units, and 10 units, respectively). Results for Intervention 2 indicated an increase in subjective distress of 25 units. Intervention 3 demonstrated no change (0 units). See Figure 22.

**PTSS**

All participants’ self-reported PTSS score from Day 2 were graphed along the x-axis of Figure 23, with their self-reported PTSS from Day 3 on the y-axis. A line representing no change from pre- to postintervention was drawn from (0, 0) to (80, 80). Results for Control 1, Control 2, Intervention 2, and Intervention 3 indicated decreases in PTSS from pre- to postintervention (39 units, 2 units, 1 unit and 3 units, respectively). Intervention 1 demonstrated no change (0 units).
Figure 22. All participants subjective distress pre- to postintervention.

Notes: C1 = Control 1, C2 = Control 2, I1 = Intervention 1, I2 = Intervention 2, I3 = Intervention 3; x-axis = difference in self-reported subjective distress from pre-Day 2 Activation Phase to highest during Day 2 Activation Phase, y-axis = difference in self-reported subjective distress from pre-Day 3 Activation Phase to highest during Day 3 Activation Phase. The solid black line represents no symptom change. Above the line indicates an increase in subjective distress reactivity following the intervention. Below the line indicates a decrease in subjective distress reactivity following the intervention.
Figure 23. All participants PTSS pre- to postintervention.

*Notes:* C1 = Control 1, C2 = Control 2, I1 = Intervention 1, I2 = Intervention 2, I3 = Intervention 3; x-axis = total self-reported PTSS from Day 2, y-axis = total self-reported PTSS from Day 3. The solid black line represents no symptom change. Above the line indicates an increase in PTSS following the intervention. Below the line indicates a decrease in PTSS following the intervention.

**Intrusions**

All participants’ self-reported intrusion scores from Day 2 were graphed along the x-axis of Figure 24, with their self-reported intrusion scores from Day 3 on the y-axis. A line representing no change from pre- to postintervention was drawn from (0, 0) to (20, 20). Results for Control 1, Control 2, Intervention 1, and Intervention 3 indicated decreases in PTSS from
pre- to postintervention (6 units, 2 units, 3 units, and 7 units, respectively). Intervention 2 demonstrated no change (0 units).

Figure 24. All participants intrusions pre- to postintervention.

Notes: C1 = Control 1, C2 = Control 2, I1 = Intervention 1, I2 = Intervention 2, I3 = Intervention 3; x-axis = self-reported intrusions from Day 2, y-axis = self-reported intrusions from Day 3. The solid black line represents no symptom change. Above the line indicates an increase in intrusions following the intervention. Below the line indicates a decrease in intrusions following the intervention.
CHAPTER 6
DISCUSSION

Research suggests that memory reconsolidation interference may be one mechanism for treating disorders involving fear memory (Brunet et al., 2008; Brunet et al., 2018; Kessler et al., 2018; Maples-Keller et al., 2017; Soeter & Kindt, 2015). These studies show that such treatment is possible with pharmacological interventions (Brunet et al., 2008; Brunet et al., 2018), yet findings are inconsistent (Wood et al., 2015) and research has identified several factors (e.g., length of memory activation, introduction of novel information) that must be considered before a treatment targeting reconsolidation interference may be effective (see Monfils & Holmes, 2018).

One particularly important boundary condition for the initiation of memory reconsolidation processes may be the occurrence of a prediction error during memory activation (see Exton-McGuinness et al., 2015 for a review; Sinclair & Barense, 2018). The occurrence of a prediction error during the memory activation cue may determine whether reconsolidation or extinction processes occur (Exton-McGuinness et al., 2015). These two processes are theoretically mutually exclusive and result in different outcomes; memory reconsolidation results in changes to the original memory (thus the return of fear phenomenon cannot occur at follow-up), while extinction results in creation of a new, competing memory (thus allowing for the return of fear phenomenon; e.g., Alberini, 2013). A behavioral intervention targets reconsolidation interference by using prediction error during memory activation to destabilize a memory, then validated methods of reconsolidation interference (i.e., the retrieval-extinction
paradigm, visuospatial interference; Monfils et al., 2009 and James et al., 2015, respectively) to impair reconsolidation of fear-based memory may provide a more effective and flexible alternative to current pharmacological and behavioral methods in the treatment of highly complex fear-memory based problems, such as PTSS. The current study designed and tested such a behavioral protocol to permanently attenuate PTSS.

The Current Study

Data from five eligible participants, two in the Control Condition and three in the Intervention Condition, were examined using single-case methods. Results of these analyses were mixed, but demonstrated promise for future iterations of the treatment paradigm. These results will be reviewed in the following sections. A summary of results can also be found in Table 3. The hypotheses tested are as follows:

H1 The Prediction Error condition (i.e., Intervention Condition) will show a decreased SUDS response during activation from Day 2 to Day 3 compared to the Full Retrieval Control condition (i.e., Control Condition).

H2 The Prediction Error condition will show a greater decrease in overall PTSS from Day 2 to Day 3 compared to the Full Retrieval Control condition.

H3 The Prediction Error condition will show a greater decrease in intrusion symptoms from Day 2 to Day 3 compared to the Full Retrieval Control condition.

H4 The Prediction Error condition will show a greater decrease in psychophysiological reactivity from Day 2 to Day 3 compared to the Full Retrieval Control condition.
Table 3

Results of Case Series Analyses

<table>
<thead>
<tr>
<th>Hypotheses</th>
<th>Day 1 Writing Phase</th>
<th>Day 2 Activation Phase</th>
<th>Day 2 Extinction Phase</th>
<th>Day 2 Extinction Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the narrative induce activation?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Did activation occur?</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Did extinction occur?</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Did extinction occur?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Did subjective distress decrease?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Did overall PTSS decrease?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Did intrusions decrease?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Did HR response decrease?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Did SC response decrease?</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Control 1 demonstrated a decreased SC response; however, this decrease may be attributed to increased data variability as opposed to a true decrease.
Preliminary Analyses

Results of preliminary analyses indicate several probable failures of the treatment protocol. One inconsistent result was the success, or lack thereof, of the Day 1 Writing Phase (~A) to produce a narrative that resulted in activation. Accelerating subjective distress was observed for both Control Condition participants and Intervention 3. Results for Intervention 1 were inconclusive, and Intervention 2 actually demonstrated a decelerating trend. Overall, the effectiveness of the writing task to engender demonstration of activation appears unrelated to the actual effectiveness of the activation task. Despite the apparent effectiveness of the writing task for the control participants and Intervention 3, strong evidence of activation during the Day 2 activation phase was observed only for Intervention 1 with mixed but generally supportive evidence for activation for Control 1 and Intervention 3 and mixed but generally supportive evidence against activation for Control 2 and Intervention 2. Although extinction during this phase was only expected for Control Condition participants, all participants demonstrated some level of extinction, although the evidence for extinction was admittedly strongest for the Control Condition participants and Intervention 2. Finally, extinction was expected for all participants during the Day 2 Extinction Phase. No Control Condition participant demonstrated extinction during this phase, and all intervention condition participants demonstrated mixed results with at least some level of extinction represented.

No clear pattern is observable in the results as described above, yet the beginnings of a pattern do emerge. Of the Control Condition participants, only Control 1 demonstrated the expected pattern of results for the Day 2 Activation Phase, including evidence of activation and extinction. Control 2’s evidence of activation is less convincing though not absent, and although
evidence of extinction during this phase was stronger for Control 2 than for the Intervention Condition participants (except for Intervention 2), it is difficult to argue for the presence of extinction when activation cannot be adequately determined.

Of the Intervention Condition participants, both Intervention 1 and Intervention 3 demonstrated evidence of the expected pattern of results for the Day 2 Activation Phase. Both participants demonstrated evidence of activation during this phase, and although they also demonstrated some level of extinction, the evidence was less strong than that of the Control Condition participants. Interestingly, Intervention 2 demonstrated a pattern more similar to the Control Condition participants, and especially Control 2. Namely, evidence for activation was poor, and evidence of extinction was strong, albeit the same concern for the interpretation of this evidence exists for Intervention 2 as it does for Control 2.

It is perhaps not surprising that the evidence of activation for Intervention 2 is so poor; of all participants, only Intervention 2 demonstrated decreased subjective distress during the Day 1 Writing Phase (~A). It is possible that Intervention 2’s trauma narrative was not sufficient to induce activation from the beginning, thus leading to an activation task during the Day 2 Activation Phase that failed to induce reconsolidation processes, just as the control participants’ tasks were designed to prevent these processes. The lack of an activating effect of the narrative may be attributable to avoidance; however, it is also possible that poor sleep interfered with the effectiveness of the paradigm. Intervention 2 was the only participant who consistently reported less than 7 hours of sleep per night on the PSQI (~5 hours), and research has demonstrated a damaging effect of sleep deprivation on memory reconsolidation, extinction, and prediction error signaling (Spoormaker et al., 2012; Stickgold & Walker, 2007). However, it may be relevant to note individual similarities between Intervention 2 and Control 2 specifically, as Intervention 2
was most similar to Control 2, and Control 2 demonstrated a somewhat different pattern of results from Control 1. One similarity is immediately apparent. Control 2 and Intervention 2 were the only two participants whose initial PCL-5 score was categorized in the “severe” range (51+; 63 and 68 respectively). Control 1, Intervention 1, and Intervention 3 were all categorized as “moderate” severity (41 – 50; 42, 49, and 46, respectively). It is possible that symptom severity, or factors related to symptom severity, may represent a boundary condition for this paradigm such that participants with more severe symptoms are less likely to experience sufficient activation during the activation cue due to increased avoidance behaviors or some other relevant factors.

It is also interesting to note that the Day 2 Extinction Phase did not result in evidence of extinction for either Control Condition participants and mixed evidence at best supporting extinction for all Intervention Condition participants. It is unclear why the extinction task was not more effective at engendering an extinction response. It is possible that an audio exposure task simply allows too much room for avoidance; the participants may have been able to “tune out” the recording or distance themselves from the narrative more effectively since their engagement with the narrative during this phase was passive. Regardless, it is noteworthy, if unexpected, that the Day 2 Extinction Phase was likely more effective for the Intervention Condition participants than for the Control Condition participants. Perhaps the inclusion of a prediction error during the activation task was successful at destabilizing aspects of the trauma memory, resulting in increased ability to engage with an extinction protocol. The prediction error may have increased susceptibility to the novel information presented during the extinction task, as the emotional content of the original memory was being attenuated and not suppressed, and the new information incorporated into the existing memory as opposed to creating a new and
competing memory. However, this finding was not hypothesized, and more research is needed to reproduce and explore the potential extinction enhancing effects of similar reconsolidation interference paradigms.

H1

H1 predicted that the Intervention Condition participants, or the Prediction Error condition as described previously, would demonstrate decreased subjective distress during the Day 3 Activation Phase (B’) compared to the Control condition (the Full Retrieval Control condition). For the purposes of this study, the Day 1 Writing Phase (~A) and the Day 2 Extinction Phase (~A’) are being used as pseudobaselines for the subjective distress data, as both phases required prolonged exposure to the details of the participants’ trauma memory. However, significant differences in protocol (i.e., a single exposure to the full memory via a written task for the Day 1 Writing Phase versus repeated exposure to an identified “worst section” of the trauma memory via audio for the Day 2 Extinction Phase) may prevent any true comparison using traditional single-case design, and examination of the details of the findings is inappropriate outside the larger context of the other outcomes. Therefore, such an exploration will not happen here. Instead, these details will be explored later where appropriate. However, using the technique pioneered by the behavior analyst Neville Blampied (2000, 2011) of the University of Canterbury, New Zealand, a general overview of the data sufficient to address H1 can be accomplished. Visual analysis reveals no clear pattern in the data (Figure 22). The participant with the greatest improvement in subjective distress from the Day 2 Activation Phase (B) to the Day 3 Activation Phase (B’) was Control 2, with both Control 1 and Intervention 1
demonstrating more modest improvement. Intervention 3 demonstrated virtually no change, while Intervention 2 appeared to experience an increase in distress.

The immediate conclusion that can be drawn is that the paradigm was not successful at decreasing subjective distress. If anything, the Control condition participants experienced more reliable decreases than the Intervention condition. Likely, this is an artifact of the study design; the Control condition was not an inactive control, so some decrease in distress is expected. What was unexpected is the relative lack of decrease for the Intervention condition. Intervention 1’s decrease was comparable to Control 1’s, where Intervention 2 demonstrated no change and Intervention 3’s change was negative. It is possible that these findings reflect individual differences in distress tolerance, use of avoidance behaviors, understanding or interpretation of the SUDS measure, or some other factor. For example, if Intervention 2 engaged in more avoidance behavior on Day 2 than the other participants, the increase in their subjective distress may not represent an actual increase in distress but rather a decrease in avoidance. The other participants, having engaged in less avoidance, would exhibit results more reflective of changes in distress (or lack thereof). Such avoidance may help explain Intervention 2’s unusual decrease in distress on Day 1 as well.

However, it is also possible that these findings reflect a failure of the paradigm; where Intervention 1’s results were similar to the improvement seen in the controls, Intervention 2 and 3’s results may be indicative of spontaneous recovery. If the paradigm was unsuccessful at initiating reconsolidation processes for the Intervention Condition participants, then any decreases in distress during the exposure task were likely due to extinction processes, i.e., new learning that leaves open the possibility of the reemergence of the old memory. Individual differences in susceptibility to the return of fear phenomenon are documented (Lonsdorf & Merz,
2017), so it would not be unexpected that some participants would maintain treatment gains while others revert to their initial distress levels or even increase over time. As such, the findings of the current study may suggest that the paradigm failed to initiate reconsolidation processes to augment the subjective distress of the participants.

H2

H2 predicted that the Prediction Error (Intervention) condition would demonstrate a greater decrease in overall PTSS from Day 2 to Day 3 compared to the Full Retrieval (Control) condition. The lack of baseline data and the low number of timepoints limit what information can be gleaned using traditional case series analyses. Therefore, the Blampied (2011) technique was again utilized (Figure 23), with results of the traditional case series analyses examined where appropriate. Using the Blampied (2011) technique, only Control 1 demonstrated a response to treatment (i.e., a decrease in PTSS of $\geq 5$) in PTSS from Day 2 to Day 3. Control 2, Intervention 1, and Intervention 2 all demonstrated no real improvement, with Intervention 3 demonstrating a small improvement that is likely not a true response to treatment (i.e., PTSS decreased by 3). The graphs generated by the traditional case series analyses show that all participants except for Intervention 1 demonstrated a stable decelerating trend across all three days of the study. All Intervention Condition participants experienced clinically meaningful (i.e., a decrease in PTSS of $\geq 10$), decreases in PTSS between Day 1 and Day 2, prior to any intervention, with little to no change from Day 2 to Day 3, postintervention. Control 1 demonstrated no meaningful change preintervention, and Control 2 demonstrated no meaningful change at any point.

H2 was not supported; no intervention participant experienced decreases in PTSS following the intervention. In fact, the only participant to demonstrate decreased PTSS between
Day 2 and Day 3 was a Control condition participant (Control 1). The lack of any observable pattern in PTSS reductions between Day 2 and Day 3 likely indicates that the paradigm was not successful in reducing PTSS. Yet, all Intervention condition participants and no Control condition participants experienced clinically meaningful reductions prior to the intervention. It is possible that this difference represents sampling error; the randomly assigned Intervention condition participants may all have experienced more natural recovery or benefitted more from the written exposure task than the Control condition participants. If this interpretation is true, the lack of any effect of the intervention on PTSS for the Intervention condition participants may be the result of a floor effect. However, PTSS symptoms often vary from week to week, which is why diagnostic measures of PTSD assess for symptoms over the past month (e.g., the clinician-administered PTSD Scale for DSM-5; Weathers et al., 2018). It is therefore likely that these findings, as well as Control 1’s postintervention decrease, are all artifacts of natural fluctuations in symptoms. This interpretation seems especially likely considering that Control 1, Intervention 2, and Intervention 3’s fluctuations were still within their data stability envelopes, suggesting that the data were stable despite the fluctuations.

What is most revealing are the data trends; all but Intervention 1 demonstrated a stable decelerating trend, suggesting that PTSS symptoms were naturally decreasing across all three days for all participants except Intervention 1, regardless of condition. Given Intervention 1’s steep decline in symptoms prior to the intervention and the stable decelerating trend of all other participants, it is reasonable to expect that continued data collection would have revealed a stable decelerating trend for Intervention 1 as well. The sample used in this study was a nonclinical sample and PTSS symptoms can naturally decrease over time (Orcutt et al., 2014), so these results are not necessarily surprising. It is possible that a larger sample and aggregate data...
analysis would account for individual differences in symptom fluctuation, revealing more consistent averaged patterns of treatment response. However, it may be unreasonable to expect to observe real differences in self-reported symptoms within a week of an intervention regardless of method; multiple or more distal follow-up timepoints are needed to determine reliable change for both aggregate and single-case designs. Furthermore, an intervention that does not lead to observable decreases in symptoms for an individual is necessarily limited in clinical utility. The advantage of a case series design is that such limitations can be identified and quickly corrected in future iterations.

H3

H3 predicted that the Prediction Error (Intervention) condition would demonstrate a greater decrease in intrusion symptoms from Day 2 to Day 3 compared to the Full Retrieval (Control) condition. Since the measure of intrusion symptoms was a subscale of the PTSS measure, the intrusion symptoms data shared the same limitations as the overall PTSS data. Therefore, the Blampied (2011) technique was once again utilized (Figure 24), with results of the traditional case series analyses examined where appropriate. Using the Blampied (2011) technique, it was revealed that all participants except Intervention 2 experienced a decrease in intrusion symptoms between Day 2 and Day 3. Examination of the data using traditional case series analyses showed that each participant exhibited a unique pattern of responding across the three days: Control 1’s symptoms decreased at a steady rate from Day 1 to Day 3; Control 2’s symptoms increased on Day 2 and returned to Day 1 levels on Day 3; Intervention 1’s symptoms decreased across all three days with the majority of the decrease occurring between Day 1 and
Day 2; Intervention 2’s symptoms decreased only from Day 1 to Day 2; and Intervention 3’s symptoms decreased only from Day 2 to Day 3.

The individualized nature of symptom response suggests a similar interpretation for the intrusion symptom data as for the overall PTSS data. Primarily, H3 was not supported. It is likely that the observed changes in intrusion symptoms are attributable to natural week-to-week fluctuations in symptoms, not to any aspect of the paradigm. Two observations support this interpretation. First, three of the five participants (Control 1, Intervention 1, and Intervention 2) experienced symptom decrease prior to the intervention, with two of those three (Intervention 1 and Intervention 2) demonstrating most or all of their symptom decrease by Day 2. Second, all but Control 2 demonstrated stable decelerating trends across all three days, which may indicate symptom decreases are driven by either natural recovery or common exposure factors all participants shared across all three days. Control 2’s lack of a stable trend may be an artifact of data collection; it is most likely that a stable trend would have been observed with more data collection time points. However, it is also possible that Control 2’s individual characteristics lead to its difference in responding.

Control 2 was the only participant to experience an increase in intrusion symptoms on Day 2. PTSS data was collected at the beginning of each day, therefore this increase in intrusion symptoms may be attributed to the exposure Control 2 endured on Day 1. Characteristics of Control 2’s index trauma may be a driving factor; Control 2 was the only participant with an index event in which they were both a victim and perpetrator of trauma. In the interest of preserving Control 2’s confidentiality, the details of the event are be discussed, but exposure to a previously avoided perpetration memory on Day 1 may have increased the intrusions that Control 2 experienced during the following week compared to other participants. The broader
literature may support this interpretation as a positive relationship between guilt and/or shame and trauma psychopathology has been demonstrated in the literature above and beyond other factors such as fear or sadness (e.g., Matos et al., 2012; see Cunningham, 2020 for a review of the positive relationship between guilt/shame and PTSD symptom presentation and severity). Control 2’s exposure on Day 1 may have led to increased intrusion symptom severity by decreasing avoidance. The repeated exposure on Day 2 may have then promoted a decrease in intrusion symptoms that returned them to the level Control 2 reported on Day 1 when their lower level of symptoms may have been driven by avoidance. This interpretation is not to say that guilt/shame were not contributing factors for the other participants. Certainly, ample research has demonstrated the role guilt and shame may play in PTSS for victims of trauma (e.g., Cunningham, 2020). Rather, this interpretation of Control 2’s results suggests that the added complexity of the participant being both a victim and perpetrator may have heightened their experience of guilt/shame relative to the other participants. Obviously, this interpretation is conjecture. To the author’s knowledge, no study has yet been done examining differences in pathology and symptomatology of victims versus perpetrators. Regardless of interpretation, these results again demonstrate the importance of single-case designs in treatment studies. These highly varied patterns of treatment response (or nonresponse) would not be visible using aggregate techniques, and the necessary examination of individual differences affecting outcomes would be less actionable.

H4

H4 predicted that the Prediction Error (Intervention) condition would demonstrate a greater decrease in psychophysiological arousal from Day 2 to Day 3 compared to the Full
Retrieval (Control) condition. Skin conductance response is the most commonly used measure in the human memory reconsolidation literature (e.g., Björkstrand et al., 2015; Brunet et al., 2008; Hu et al., 2018; Oyarzún et al., 2012; Schiller et al., 2010; Soeter & Kindt, 2012; Wood et al., 2015), with heart rate also commonly used (e.g., Brunet et al. 2008; Wood et al., 2015), and as such both were considered the primary outcome measures for this study. The data collection procedures as originally designed resulted in data perfectly suited for traditional case series analysis (Gast & Spriggs, 2009). Therefore, it is appropriate to examine the results of these analyses both independently and within the context of the other outcome data without use of the Blampied (2011) technique.

Heart Rate

Examination of the HR data revealed three patterns of intervention response: 1) no change in responding from Day 2 to Day 3 (i.e., Control 1, Intervention 3); 2) deteriorating response from Day 2 to Day 3 (i.e., Control 2, Intervention 2); and improving response from Day 2 to Day 3 (i.e., Intervention 1). There were no clear differences between the Control and Intervention condition participants. However, the only participant to demonstrate improved heart rate response was an Intervention Condition participant (Intervention 1).

The results of the analyses using HR data suggest that the Intervention condition was not able to produce reliable decreases in spontaneous recovery compared to the Control condition. Yet, some evidence suggests that the Control condition did work as expected. Control 1 demonstrated a 0% PND on both Day 2 and Day 3, suggesting that the activation task was at no point sufficient to induce a change in HR response. However, they did demonstrate an initial increase in HR at the beginning of both Activation Phases that quickly extinguished; the increase
was just not large enough to be outside the range of the baseline phases. This consistent pattern of small, abrupt increases in HR that quickly decelerated may suggest Control 1 experienced spontaneous recovery of HR response on Day 3 as expected for a Control condition participant. This interpretation is tenuous, as neither abrupt increase was outside the range of the baseline data. As such, it is possible that this increase was due to data variability. Yet, this second interpretation seems unlikely. The presence of an increase in HR at the onset of the Activation Phases on both days suggests a pattern most likely related to the onset of the phases, as it seems unlikely that data variability alone would create a consistent pattern across both days. The clear evidence of spontaneous recovery for Control 2 above and beyond their preintervention HR response bolsters the claim that the Control condition worked as expected. The intervention without prediction error was unable to prevent spontaneous recovery in either Control condition participant.

The results for the Intervention condition participants were mixed. Intervention 2 demonstrated a response pattern most similar to Control 2; HR response deteriorated from Day 2 to Day 3. Perhaps it is not surprising that Intervention 2 did not see the expected pattern of responding for an Intervention condition participant. Intervention 2 demonstrated unusual response to their narrative during the Day 1 Writing Phase (~A) as well as a unique pattern of responding for the outcome measures for H1 and H3 (i.e., subjective distress and intrusion symptoms, respectively). Intervention 2 may have produced a narrative on Day 1 that was insufficiently activating, possibly due to engagement in relatively higher levels of avoidance or due to the detrimental effects of sleep deprivation (Spoormaker et al., 2012; Stickgold & Walker, 2007). That insufficiently activating narrative may have led to insufficient activation during the Day 2 Activation Phase to destabilize the memory, followed by prolonged audio exposure during
the Day 2 Extinction Phase that likely engaged extinction mechanisms since destabilization had not occurred. If this interpretation were accurate, the expected outcome for Intervention 2 would be similar to that of the Control condition participants. Such an outcome was observed, suggesting that the intervention for Intervention 2 failed to induce memory reconsolidation processes.

Intervention 3 had a surprising pattern of HR responding. Although they demonstrated 0% PND on both days, and therefore no observed changes from Day 2 to Day 3, they also demonstrated a consistent pattern of abrupt change in HR at the onset of both Activation Phases. Like the pattern observed for Control 1, this pattern suggests the activation task and not data variability is likely the cause of this observed change. Unlike Control 1, the abrupt observed change was a decrease in HR response. It is unclear why a decrease such as this might occur. One possible explanation may be the presence of an unexpected confound: anticipatory anxiety. Intervention 3 may have been relatively more sensitive to anticipatory anxiety than the other participants, which may have resulted in higher HR during the baseline phases and relief once the audio actually began. The presence of heightened worry/anticipatory anxiety may explain why Intervention 3’s HR data was different from all other participants, while no other patterns unique to Intervention 3 were observed for any other outcome. Some research suggests that increased HR is uniquely a psychophysiological correlate for worry and anticipatory anxiety compared to neutral controls and performance anxiety (e.g., Hofmann et al., 2005; Thayer & Brosschot, 2008), although this literature is mixed (e.g., Wilhelm et al., 2001). Research also suggests that this relationship with worry and anticipatory anxiety may not be present for other measures such as SC compared to neutral controls (e.g., Delgado et al., 2009; Wilhelm et al., 2001) and subjective distress compared to neutral controls and performance anxiety conditions.
(Hofmann et al., 2005). Intervention 3’s data appear to follow the pattern demonstrated in the literature; HR data decreased after the baseline phases suggesting anticipatory anxiety during those phases, and that pattern was not observed for SC (see the next section) or subjective distress (see the earlier section regarding H1). Worry/anticipatory anxiety may therefore have been a confound for Intervention 3 that interfered with their HR data. Future iterations of this project should work to control for individual differences in worry/anticipatory anxiety and further examine the possible effects of this confound on the intervention.

The only participant to show a decrease in responding on Day 3, and thus evidence of an intervention successful at preventing spontaneous recovery, was Intervention 1. In the broader literature, a lack of spontaneous recovery following a reconsolidation paradigm compared to controls is widely considered indicative of successful interference of reconsolidation processes (e.g., Björkstrand et al., 2015; Brunet et al., 2008; Brunet et al., 2018; Hu et al., 2018; Oyarzún et al., 2012; Schiller et al., 2010; Soeter & Kindt, 2012; Wood et al., 2015). The HR results for Intervention 1 compared to the controls may therefore represent evidence of a successful paradigm for this participant. This interpretation is not certain or especially convincing; however, considering the failure of the paradigm for both other Intervention condition participants. Considering the individual differences between participants that provide possible explanations for Intervention 2 and Intervention 3’s unexpected results (i.e., an insufficiently activating narrative and high anticipatory anxiety, respectively), it is not unreasonable to suggest that Intervention 1’s HR results may indicate that the intervention was successful for this one participant. However, the failure to replicate this result for any other Intervention condition participant prevents firm conclusions and may just as reasonably suggest that the intervention paradigm was not successful at decreasing HR response, compared to controls. Regardless, the
utilization of a single-case design allowed for closer examination of individual differences that may have contributed to these differential results than would have been possible using aggregate techniques. This information will be invaluable for creating more successful future iterations of this treatment paradigm.

**Skin Conductance**

Examination of the SC data revealed two patterns of responding: 1) a deterioration of SC from Day 2 to Day 3 (i.e., Control 2, Intervention 2); and 2) an improvement of SC from Day 2 to Day 3 (i.e., Control 1, Intervention 1, Intervention 3). There are no clear differences between the Intervention and Control conditions. However, of the three participants who demonstrated improvement of SC on Day 3, only Control 1 demonstrated increased data variability, suggesting that their reported decrease in SC on Day 3 may not represent an actual decrease.

Both Control 2 and Intervention 2 demonstrated evidence of spontaneous recovery. For the Control condition participant, this was expected. For Intervention 2, this was unexpected, however it may not be surprising considering the uniqueness of Intervention 2’s responding across most of this study’s outcome measures. As described above, individual differences in factors such as avoidance behavior and sleep may have resulted in Intervention 2 not engaging in sufficient activation during their activation tasks to induce memory destabilization. Thus, they may have engaged extinction processes instead, as described above, resulting in SC outcomes more similar to Control condition participants.

Surprisingly, Control 1 demonstrated a decrease in SC response, as evidenced by a 25% decrease in PND on Day 3 compared to Day 2. However, Control 1 also demonstrated increased data variability at the initiation of the Day 3 Activation Phase (B), preventing any clear
interpretation of the change in data levels. Although it’s possible that Control 1 demonstrated improvement in SC response, any changes in data are more likely attributable to this increase in instability due to the intervention. Closer examination of data patterns can provide a clearer picture of this instability; Control 1 experienced a large, abrupt increase in SC at the onset of the Day 3 Activation Phase (B) that rapidly decelerated, resulting in high data variability. This pattern of variability may suggest that spontaneous recovery occurred, followed by rapid extinction. It does not appear to suggest that Control 1’s initial reaction was diminished, only that their rate of deceleration was heightened.

Unlike Control 1, both Intervention 1 and Intervention 3 demonstrated data stability, allowing for interpretation of changes in PND and data parameters. Intervention 1 demonstrated a stable 18% PND decrease, and Intervention 3 demonstrated a stable 60% decrease. The fact that the only participants to demonstrate a stable decrease in SC from Day 2 to Day 3 were Intervention condition participants may provide some evidence that the intervention was successful at attenuating spontaneous recovery of SC response. Unfortunately, Control 1’s results prevent firm conclusions; however, their increased data variability due to the Day 3 Activation Phase suggests a response clearly different from Intervention 1 and Intervention 3. Where Intervention 1 and 3 show clear decreases in responding, Control 1 shows a large increase and rapid decrease.

Summary

Hypotheses H1, H2, and H3 were not supported. There were mixed results for H4, with some evidence suggesting more of an effect for some of the Intervention condition participants (Intervention 1 and 3), but these effects were small and not consistent between or within
participants. Looking at individual participants, the most consistent improvement was seen for Intervention 1, who demonstrated improvement in subjective distress, intrusion symptoms, and both HR and SC response. Second, Intervention 3 demonstrated a small improvement in overall PTSS, an improvement in intrusions, and an improvement in SC response. Third, Control 1 demonstrated improvement in subjective distress, PTSS, and intrusion symptoms, and an increase in SC response variability. Fourth, Control 2 demonstrated an improvement in subjective distress and a deterioration in HR and SC response. Finally, Intervention 2 demonstrated a deterioration in subjective distress and both HR and SC response. No other changes in outcomes were observed.

Preliminary analyses suggest that Intervention 2 may not have engaged in sufficient activation to induce memory destabilization, thus it is not surprising that their results are more similar to, and perhaps worse than, those of the Control condition participants. Furthermore, examination of patterns in the data suggest that any improvement in PTSS and intrusion symptoms for all participants were likely a result of natural recovery. Therefore, most of the improvement observed for Intervention 3 and Control 1 was likely not due to the intervention; for these participants, only Intervention 3’s SC response and Control 1’s subjective distress indicates actual postintervention improvement. In considering only the primary outcome measures for this study and the broader literature (i.e., SC and HR; e.g., Brunet et al., 2008), only Intervention 1 and Intervention 3 demonstrated clear improvement. The results of this study therefore suggest that the intervention may have had some effect, suggesting the paradigm may have been successful at utilizing memory reconsolidation processes. However, this effect was neither strong nor consistent enough to suggest the intervention has clinical utility in its current iteration.
Conclusions

The results of this study make one thing clear; the intervention did not work. Regarding specific hypotheses, H1, H2, and H3 were not supported. Yet, H4’s results were mixed, suggesting partial, if limited, support. The lack of clear differences between conditions for H1, H2, and H3 may be reflective of both conditions requiring participants to decrease avoidance behavior. Decreasing avoidance is the primary goal of current trauma-focused interventions (e.g., Foa & Rothbaum, 1998); as such, the lack of differences between the two conditions in this study may suggest that both conditions targeted avoidance equally successfully. The findings regarding H4 may indicate that the result of this approach behavior was extinction learning for the Control condition and memory updating for the Intervention condition. Although this outcome is promising, as it suggests that the paradigm may be successfully targeting memory reconsolidation in the context of PTSS, the results regarding the other hypotheses indicate that this paradigm does not yet have clinical utility beyond that of any treatment that targets avoidance.

Changing data analytic procedures following the COVID-19 pandemic was a difficult task, but doing so may have provided an opportunity to explore a technique uniquely suited to the task of translating basic science into a clinical intervention. Individual differences in avoidance behaviors, sleep, anticipatory anxiety sensitivity, etc. may play a larger role in this intervention’s effectiveness than anticipated. Future iterations of this study should continue to use single-case designs to examine the effects of these differences and experiment with techniques for controlling for them. Further, the failure to detect differences between conditions using self-report measures and the partial support of an intervention effect using
psychophysiological measures may suggest the need to reconsider the measures being used. Perhaps self-report measures such as the PCL-5 and SUDS are less sensitive to the changes one would expect following this intervention; either it is unreasonable to expect PTSS and distress to change meaningfully after a single-session intervention or the subjective nature of participant responding on these measures limits their utility. For example, a participant may complete the PCL-5 not based on the actual symptoms they experienced in the past week, but on the experiences they believe they typically experience on any given week. Changes in PCL-5 scores may therefore represent changes in the attention paid to their symptoms week to week, as opposed to actual symptom change.

But the differences in results depending on the type of measure used may also reveal one important question: how do you define a memory? Any definition of a memory is necessarily a practical one. In reality, discreet memories do not truly exist; rather, what is often thought of as a memory is more a network of connected episodic, semantic, sensory, visual-spatial, and emotional memories. The definition of a memory is defined by the level of analysis. In targeting “a memory” in the current study, the level of analysis was intended to be at the level of emotional memory versus episodic memory; the study sought to augment emotional memory while leaving episodic memory intact. However, the definition of memory actually used was at a higher level of scale; the target memory was a partial narrative of the full event. This mismatch between the goal of the study and the way memory was defined may have led to the creation of an activation cue that lacked specificity to consistently destabilize the true target. Other research has attempted to increase the specificity of their activation cues by targeting the memories related to specific intrusions (Kessler et al., 2018) or limiting the cue to 30 seconds (Brunet et al.,
2008, 2018) with some success. Future iterations of this study may consider using similar techniques or exploring other practical definitions for the memories being targeted.

Considerations Due to the COVID-19 Pandemic

Due to the unexpected global health crisis of the 2020 COVID-19 pandemic, data collection for the current study had to be abruptly halted indefinitely after data from only five participants who met all inclusion criteria were collected. This halt to data collection was a university-wide decision initiated concomitantly with the state-wide stay-at-home order for the state of Illinois. Following this initial decision, the university further decided that, for the safety of both participants and researchers, face-to-face data collection was prohibited indefinitely, but at least through the next Fall semester, for all but select studies that were able to meet strict guidelines for social distancing and use of personal protective equipment. Due to the reliance on psychophysiological recording equipment, close contact with participants is a necessary component of this study and thus data collection remained halted. In the interest of continued progress within this program of research, as well as to address the practical concern of timely completion of this doctoral dissertation, alterations to the initial dissertation proposal that 1) protected the integrity of the study, 2) sufficiently answered all research questions, and 3) allowed for uninterrupted research and training progress were explored. It was determined that examination of all currently collected data within a single-case experimental design would meet all three of these requirements. Furthermore, after careful consideration of this change to the dissertation proposal, it is my view that a single-case experimental design may in fact be a more appropriate design for the initial purposes of this study than what was originally proposed.
Single-Case Designs for the Development of Novel Interventions

The general purpose of the current study was to establish behavioral procedures for memory reconsolidation interference as part of a program of research seeking to translate findings from basic memory reconsolidation literature and the fledging applied memory reconsolidation literature to clinical application in the treatment of PTSS. Although the intervention was a failure, the use of a case series design was a success. Substantial information was gathered to inform the next iteration of this study (Appendix C), providing clear future directions for research. The initial design of the study was a randomized, controlled experiment in which aggregate data from 20 intervention condition participants would be compared to the aggregate data from 20 control condition participants. Although such a design is common when developing novel treatments, there are several reasons a single-case design is a more appropriate, if often overlooked, method of study for treatment development. These reasons include efficiency, ethics, improved demonstration of treatment effectiveness and efficacy, and the clearer distinction between statistical and clinical significance.

First, in the development of a novel treatment, efficiency is key, especially during the early stages of development. The translation of research findings from basic science and other areas of applied science to a novel use is notoriously difficult and nonlinear. Such research typically involves several iterations of protocol design, experimentation, protocol redesign, experimentation, etc. before theoretically consistent, empirically validated and reliable results may be produced. Relying on aggregate methods of study design, such as randomized controlled trials, often requires a year or more of data collection per iteration to achieve large enough sample sizes for analyses. The multiple iterations often necessary for creating and fine-tuning a
novel treatment protocol therefore means data collection may take several years before the ideal, or close-to-ideal, protocol is produced, if at all. An easy way to decrease the time from project inception to usable protocol is to use a series of single-case design studies to quickly and efficiently test several iterations of a protocol in a much shorter timeframe. Using a single-case design, a researcher can test a protocol on three to five participants, examine the data and change the protocol accordingly, test the updated protocol on another three to five participants, etc. in the time it would take any aggregate method to collect the dozens of participants necessary for a single iteration. In this way, single-case experimental designs allow for scientifically rigorous but expedite methods for the development of protocols that can later be tested on larger populations once their effectiveness has been consistently demonstrated on a smaller scale.

In the development of novel treatments, researchers should be aware of one major ethical concern: the treatment is unlikely to work for the first or first several iterations. This means that when using aggregate methods of data collection and analysis, dozens of individuals may be exposed to the stressors of the study with little to no benefit. However, such research must be done if new treatments are to be developed. Researchers should therefore be mindful of this ethical concern and choose methods that minimize any risk or negative impact to participants. Single-case experimental designs can help minimize this risk by dramatically decreasing the number of participants that may need to be exposed to flawed and ineffectual iterations of study protocols before a usable protocol is established.

Finally, single-case designs are the only methods of analysis that allow for detailed examination of the effects of an intervention on the level that practitioners actually care about: the level of the individual. There are many inherent problems with the use of aggregate analytic techniques in the applied sciences (Blampied, 2000, 2011; Chiang et al., 2015; Grandy et al.,
Such techniques rely on one key, but flawed, assumption; one can draw inferences from group data to individuals. Often, this assumption is inappropriate. In the applied sciences, “groups” are often loosely defined, and it has been argued that in many cases the only similarity between all members of a group is that they have been averaged together within that group (e.g., Sidman, 1960). For example, consider a group labeled “People with PTSD.” Within this group are individuals with one of 17+ traumatic experiences (Weathers et al., 2013), with 636,120 distinct possible combinations of symptoms (Galatzer-Levy & Bryant, 2013). Because of the absurd number of combinations of traumatic experiences and symptom presentations, the only factor that can be said to be the same across all, maybe even across most, of the participants is that they were all included in the same group labeled “People with PTSD.” It is therefore problematic to expect that because the treatment appeared to work in the aggregate, it should work for any one individual, considering the lack of established connection between the individuals in the group. This fact becomes especially problematic when you consider that aggregate data analyses produce results that reflect an abstract, hypothetical “prototypical” person for that group (e.g., Sidman, 1960). For example, the mean on any measure for a group does not reflect the mean for any actual individual within that group. Instead, it reflects the mean for a “prototypical” person within that group. The statistics produced by any aggregate analysis, when taken together, likely do not reflect the statistics for any actual person. Therefore, applying the results from aggregate analyses to individual patients requires the practitioner to accept as appropriate the assumption that their patient sufficiently approximates across all relevant factors the imaginary prototypical person representing the group labeled “People with PTSD.” The implicit acceptance of this assumption by researchers greatly limits applied science’s ability to create interventions that are
effective for individuals in the real world. It is no wonder that the field, and evidence-based medicine in general, is plagued by well-documented problems of ecological validity and diminishing effect sizes (see Baker, 2016; Greenhalgh et al., 2014; Pietschnig et al., 2019; Shedler, 2018). These failures of applied science to produce results that translate directly to the real world may be partly behind continued resistance to efforts to disseminate evidence-based practices (Baker, McFall, & Shoham, 2008).

The problems with applying the results from aggregate data to individuals are not relevant to single-case designs. With single-case designs, researchers can examine the effect of interventions on individuals and compare these effects across individuals. Differences that may affect outcomes can be examined, and replication of findings produces robust results that can be directly translated for clinical use from real individuals in the lab to real individuals in the “real world.” Because study methods occur on the individual level, all study procedures can be directly translated to clinical practice and outcomes monitored using the same techniques as the research on which the clinical practice is based. Adjustment for individual differences becomes easier as the methods for monitoring the effects of any adjustment and the metrics by which outcomes are measured remain consistent from research to practice. This argument is not to say that there is no clinical use for aggregate data; it is certainly important to examine the effects of interventions for larger groups in many cases. However, single-case designs are superior in their ability to translate from lab to practice; they do not fall for the fallacy inherent in aggregate designs of confusing statistical significance with clinical significance.
REFERENCES


Gotthard, G. H., & Gura, H. (2018). Visuospatial word search task only effective at disrupting declarative memory when prediction error is present during retrieval. *Neurobiology of Learning and Memory, 156*, 80-85. https://doi.org/10.1016/j.nlm.2018.11.003


*Psychological Medicine, 38*(4), 467. https://doi.org/10.1017/S0033291707001353

Orcutt, H. K., Bonanno, G. A., Hannan, S. M., & Miron, L. R. (2014). Prospective trajectories of 
posttraumatic stress disorder in college women following a campus mass shooting. 


pharmacologic perspectives on the treatment of posttraumatic stress disorder. In M. H. 
Pollack, M. W. Otto, & J. F. Rosenbaum (Eds.), *Challenges in clinical practice: 
Pharmacologic and psychosocial strategies* (pp. 219-260). Guilford.

Oyarzún, J. P., Lopez-Barroso, D., Fuentemilla, L., Cucurell, D., Pedraza, C., Rodriguez- 

PTSD and PTSD symptoms: A meta-analytic review. *Journal of Anxiety Disorders, 
27*(1), 33-46. https://doi.org/10.1016/j.janxdis.2012.08.004

https://doi.org/10.1016/j.cpr.2009.05.001

https://doi.org/10.1016/j.tics.2015.08.003

Pedreira, M. E., & Maldonado, H. (2003). Protein synthesis subserves reconsolidation or 
extinction depending on reminder duration. *Neuron, 38*(6), 863-869.

expected and what actually occurs triggers memory reconsolidation or extinction. 
*Learning and Memory, 11*(5), 579-585.


Valsiner, J. (1986). Between groups and individuals. In J. Valsiner (Ed.), *The individual subject and scientific psychology* (pp. 113-151). Springer.


Randomization Checks

The First ANCOVA

As a randomization check, increase in SUDS ratings from the beginning of the Day 1 Writing Phase to the highest during that phase will be examined by condition to assess for differences between conditions in subjective response to the writing task prior to any manipulation. To conduct this randomization check, two planned contrasts in the context of the First ANCOVA will be examined: [(Prediction Error condition highest SUDS during the Day 1 Writing Phase) – (Prediction Error condition SUDS at the beginning of the Day 1 Writing Phase)]; and [(Full Retrieval Control condition highest SUDS during the Day 1 Writing Phase) – (Full Retrieval Control condition SUDS at the beginning of the Day 1 Writing Phase)]. It is expected that no differences in change in SUDS will be found between conditions (i.e., there will be no difference in subjective reaction to the writing task between conditions).

Additionally, SUDS at the beginning of the Day 2 Activation Phase will be examined by condition to assess for differences in subjective distress immediately prior to the manipulation. To conduct this randomization check, a planned contrast in the context of the First ANCOVA will be examined: [(Prediction Error condition SUDS at the beginning of the Day 2 Activation Phase) – (Full Retrieval Control condition SUDS at the beginning of the Day 2 Activation Phase)]. It is expected that no differences in SUDS ratings will be found between conditions (i.e., there will be no difference in subjective distress between conditions prior to the manipulation).
The Second ANCOVA

Change in overall PCL-5 scores from the Day 1 Questionnaire Phase to the Day 2 Questionnaire Phase will be examined to determine if there are differences between conditions in natural recovery from overall PTSS prior to intervention. To conduct this randomization check, two planned contrasts in the context of the Second ANCOVA will be examined: [(Prediction Error condition mean Day 2 Questionnaire Phase PCL-5 scores) – (Prediction Error condition mean Day 1 Questionnaire Phase PCL-5 scores)]; and [(Full Retrieval Control condition mean Day 2 Questionnaire Phase PCL-5 scores) – (Full Retrieval Control condition mean Day 1 Questionnaire Phase PCL-5 scores)]. It is expected that there will be no differences between conditions in change in overall PCL-5 scores between Day 1 and Day 2 (i.e., there will be no differences in natural recovery of overall PTSS).

As another randomization check, mean overall PCL-5 scores from the Day 1 Questionnaire Phase will be examined across conditions to determine if there are differences between conditions in initial overall PTSS. To conduct this randomization check, a planned contrast in the context of the Second ANCOVA will be examined: [(Prediction Error condition mean Day 1 Questionnaire Phase PCL-5 scores) – (Full Retrieval Control condition mean Day 1 Questionnaire Phase PCL-5 scores)]. It is expected that there will be no differences between conditions in Day 1 Questionnaire Phase overall PCL-5 scores (i.e., there will be no differences in initial overall PTSS).
The Third ANCOVA

Change in PCL-5 Intrusions scale scores from the Day 1 Questionnaire Phase to the Day 2 Questionnaire Phase will be examined to determine if there are differences between conditions in natural recovery from intrusion symptoms prior to intervention. To conduct this randomization check, two planned contrasts in the context of the Third ANCOVA will be examined:

\[
(Prediction \text{ Error condition mean Day 2 Questionnaire Phase PCL-5 Intrusions scale scores}) - (Prediction \text{ Error condition mean Day 1 Questionnaire Phase PCL-5 Intrusions scale scores})
\]

and

\[
(Full \text{ Retrieval Control condition mean Day 2 Questionnaire Phase PCL-5 Intrusions scale scores}) - (Full \text{ Retrieval Control condition mean Day 1 Questionnaire Phase PCL-5 Intrusions scale scores})
\].

It is expected that there will be no differences between conditions in change in PCL-5 Intrusions scale scores between Day 1 and Day 2 (i.e., there will be no differences in natural recovery of intrusion symptoms between conditions).

As another randomization check, mean PCL-5 Intrusions scale scores from the Day 1 Questionnaire Phase will be examined across conditions to determine if there are differences between conditions in initial intrusion symptoms. To conduct this randomization check, a planned contrast in the context of the Third ANCOVA will be examined:

\[
(Prediction \text{ Error condition mean Day 1 Questionnaire Phase PCL-5 Intrusions scale scores}) - (Full \text{ Retrieval Control condition mean Day 1 Questionnaire Phase PCL-5 Intrusions scale scores})
\].

It is expected that there will be no differences between conditions in Day 1 Questionnaire Phase mean PCL-5 Intrusions scale scores (i.e., there will be no differences in initial intrusion symptoms).
The Fourth ANCOVA

Mean HR during the Day 2 Baseline Phase will be examined to test for differences between conditions in baseline HR prior to any manipulation. To conduct this randomization check, a planned contrast in the context of the Fourth ANCOVA will be examined: \[ (\text{Prediction Error condition mean HR during the Day 2 Baseline Phase}) - (\text{Full Retrieval Control condition mean HR during the Day 2 Baseline Phase}) \]. It is expected that there will be no differences between conditions in mean HR during the Day 2 Baseline Phase (i.e., there will be no differences in initial HR).

The Fifth ANCOVA

The highest SC during the Day 2 Baseline Phase will be examined across conditions to test for differences between conditions in highest SC prior to any manipulation. To conduct this randomization check, a planned contrast in the context of the Fifth ANCOVA will be examined: \[ (\text{Prediction Error condition highest SC from the Day 2 Baseline Phase}) - (\text{Full Retrieval Control condition highest SC from the Day 2 Baseline Phase}) \]. It is expected that there will be no differences between conditions in highest SC from the Day 2 Baseline Phase (i.e., there will be no differences in initial SC response).

Other Randomization Checks

As further randomization checks, LEC scores from the Day 1 Questionnaire Phase, PSQI scores from the Day 1 questionnaire Phase, and gender will be examined across conditions to determine if there are differences between conditions in initial overall trauma exposure on initial sleep quantity and quality. Independent sample \( t \) tests will be used to conduct these
randomization checks. It is expected that there will be no differences between conditions in Day 1 Questionnaire Phase LEC scores, PSQI scores, or gender (i.e., there will be no differences in initial overall trauma exposure, initial sleep quality and quantity).

Paradigm Checks

The First ANCOVA

As a paradigm check, change in SUDS from the beginning of the Day 2 Activation Phase to the highest during the Day 2 Activation Phase will be examined. This paradigm check will be used to determine if the memory was sufficiently activated to induce a subjective response in all conditions. To conduct this paradigm check, two planned contrasts in the context of the First ANCOVA will be examined: 

\[(\text{Prediction Error condition highest SUDS during the Day 2 Activation Phase}) \text{ – (Prediction Error condition SUDS from the beginning of the Day 2 Activation Phase)}\]; and 

\[(\text{Full Retrieval Control condition highest SUDS during the Day 2 Activation Phase}) \text{ – (Full Retrieval Control condition SUDS from the beginning of the Day 2 Activation Phase})\].

It is expected that there will be a significant increase in SUDS from the beginning of the Day 2 Activation Phase to the highest during the Day 2 Activation Phase for both of the conditions (i.e., both conditions will report a significant increase in distress, which would be indicative of memory activation).

As another paradigm check, change in SUDS from the highest during the Day 2 Activation Phase to the end of the Day 2 Activation Phase will also be examined to assure that extinction did not occur during activation. To conduct this paradigm check, two planned contrasts in the context of the First ANCOVA will be examined: 

\[(\text{Prediction Error condition}} \text{ – (Prediction Error condition SUDS from the beginning of the Day 2 Activation Phase}))\]; and 

\[(\text{Full Retrieval Control condition highest SUDS during the Day 2 Activation Phase}) \text{ – (Full Retrieval Control condition SUDS from the beginning of the Day 2 Activation Phase})\].

It is expected that there will be a significant decrease in SUDS from the highest during the Day 2 Activation Phase to the end of the Day 2 Activation Phase for both of the conditions (i.e., both conditions will report a significant decrease in distress, which would be indicative of memory extinction).
SUDS at the end of the Day 2 Activation Phase) – (Prediction Error condition highest SUDS during the Day 2 Activation Phase); and [(Full Retrieval Control condition SUDS at the end of the Day 2 Activation Phase) – (Full Retrieval Control condition highest SUDS during the Day 2 Activation Phase)]. It is expected that there will be no change in subjective distress from highest during memory activation to the end of memory activation for each of the conditions (i.e., extinction processes will not occur during memory activation).

The Fourth ANCOVA

Change in HR from the Day 2 Baseline Phase to the Day 2 Activation Phase will be examined. This paradigm check will be used to determine if the memory was sufficiently activated to induce an objective response in all conditions. To conduct the paradigm check, two planned contrasts in the context of the Fourth ANCOVA will be examined: [(Prediction Error condition mean HR during the Day 2 Activation Phase) – (Prediction Error condition mean HR during the Day 2 Baseline Phase)]; and [(Full Retrieval Control condition mean HR during the Day 2 Activation Phase) – (Full Retrieval control condition mean HR from the Day 2 Baseline Phase)]. It is expected that there will be a significant increase in HR from the Day 2 Baseline Phase to the Day 2 Activation Phase for both of the conditions (i.e., both conditions will show an increase in HR, which would be indicative of memory activation).

The Fifth ANCOVA

Change in highest SC from the Day 2 Baseline Phase to the Day 2 Activation Phase will be examined. This paradigm check will be used to determine if the memory was sufficiently activated to induce an objective response in all conditions. To conduct the paradigm check, two
planned contrasts in the context of the Fifth ANCOVA will be examined: 

\[(\text{Prediction Error condition highest SC during the Day 2 Activation Phase}) - (\text{Prediction Error condition highest SC during the Day 2 Baseline Phase})\]; and 

\[(\text{Full Retrieval Control condition highest SC during the Day 2 Activation Phase}) - (\text{Full Retrieval control condition highest SC from the Day 2 Baseline Phase})\].

It is expected that there will be a significant increase in highest SC from the Day 2 Baseline Phase to the Day 2 Activation Phase for both of the conditions (i.e., both conditions will show an increase in SC response, which would be indicative of memory activation).

Primary Analyses

The First ANCOVA

To test hypothesis H1, two planned contrasts in the context of the First ANCOVA will be examined: 

\[(\text{Prediction Error condition highest SUDS during the Day 2 Activation Phase – SUDS from the beginning of the Day 2 Activation Phase}) - (\text{Prediction Error condition highest SUDS during the Day 3 Activation Phase – SUDS from the beginning of the Day 3 Activation Phase})\]; and 

\[(\text{Full Retrieval Control condition highest SUDS during the Day 2 Activation Phase – SUDS from the beginning of the Day 2 Activation Phase}) - (\text{Full Retrieval Control condition highest SUDS during the Day 3 Activation Phase – SUDS from the beginning of the Day 3 Activation Phase})\].

It is expected that the Prediction Error condition will show a greater decrease in SUDS response between Day 2 and Day 3 compared to the Full Retrieval Control condition (i.e., prediction error during the memory activation cue will be necessary to engage memory reconsolidation processes, thus allowing for memory interference on Day 2 and elimination of
spontaneous recovery of subjective distress on Day 3 compared to a memory activation cue without prediction error).

To partially test hypothesis H3, two planned contrasts in the context of the First ANCOVA will be examined: 

\[\text{(Extinction Control condition highest SUDS during the Day 2 Activation Phase – SUDS from the beginning of the Day 2 Activation Phase) – (Extinction Control condition highest SUDS during the Day 3 Activation Phase – SUDS from the beginning of the Day 3 Activation Phase)}\]; and 

\[\text{(Full Retrieval Control condition highest SUDS during the Day 2 Activation Phase – SUDS from the beginning of the Day 2 Activation Phase) – (Full Retrieval Control condition highest SUDS during the Day 3 Activation Phase – SUDS from the beginning of the Day 3 Activation Phase)}\].

It is expected that there will be no differences between conditions in the change in SUDS response between Day 2 and Day 3 (i.e., a memory activation cue without prediction error during Day 2 will engage extinction processes and not reconsolidation processes leading to no differences in spontaneous recovery of subjective distress between that paradigm and a traditional extinction paradigm).

The Second ANCOVA

To test hypothesis H2, two planned contrasts in the context of the Second ANCOVA will be examined: 

\[\text{(Prediction Error condition mean Day 3 Questionnaire Phase PCL-5 scores) – (Prediction Error condition mean Day 2 Questionnaire Phase PCL-5 scores)}\]; and 

\[\text{(Full Retrieval Control condition mean Day 3 Questionnaire Phase PCL-5 scores) – (Full Retrieval Control condition mean Day 2 Questionnaire Phase PCL-5 scores)}\].

It is expected that the Prediction Error condition will show a greater decrease in overall PCL-5 scores from the Day 2 Questionnaire Phase to the Day 3 Questionnaire Phase compared to the Full Retrieval Control
condition (i.e., prediction error during the memory activation cue will be necessary to engage memory reconsolidation processes, thus allowing for memory interference on Day 2 and elimination of spontaneous recovery of overall PTSS on Day 3 compared to a memory activation cue without prediction error).

**The Third ANCOVA**

To test hypothesis H3, two planned contrasts in the context of the Third ANCOVA will be examined: 

$\text{(Prediction Error condition mean Day 3 Questionnaire Phase PCL-5 Intrusions scale scores)} - \text{(Prediction Error condition mean Day 2 Questionnaire Phase PCL-5 Intrusions scale scores)}$;

and 

$\text{(Full Retrieval Control condition mean Day 3 Questionnaire Phase PCL-5 Intrusions scale scores)} - \text{(Full Retrieval Control condition mean Day 2 Questionnaire Phase PCL-5 Intrusion scale scores)}$. It is expected that the Prediction Error condition will show a greater decrease in PCL-5 Intrusions scale scores from the Day 2 Questionnaire Phase to the Day 3 Questionnaire Phase compared to the Full Retrieval Control condition (i.e., prediction error during the memory activation cue will be necessary to engage memory reconsolidation processes, thus allowing for memory interference on Day 2 and elimination of spontaneous recovery of intrusion symptoms on Day 3 compared to a memory activation cue without prediction error).

**The Fourth ANCOVA**

To partially test hypothesis H4, two planned contrasts in the context of the Fourth ANCOVA will be examined: 

$\text{(Prediction Error condition mean HR during the Day 3 Activation Phase)} - \text{(Prediction Error condition mean HR during the Day 2 Activation Phase)}$; and 

$\text{(Full
Retrieval Control condition mean HR during the Day 3 Activation Phase) – (Full Retrieval Control condition mean HR during the Day 2 Activation Phase)]. It is expected that the Prediction Error condition will show a greater decrease in mean HR from the Day 2 Activation Phase to the Day 3 Activation Phase compared to the Full Retrieval Control condition (i.e., prediction error during the memory activation cue will be necessary to engage memory reconsolidation processes, thus allowing for memory interference on Day 2 and elimination of spontaneous recovery of HR on Day 3 compared to a memory activation cue without prediction error).

The Fifth ANCOVA

To partially test hypothesis H4, two planned contrasts in the context of the Fifth ANCOVA will be examined: [(Prediction Error condition highest SC during the Day 3 Activation Phase) – (Prediction Error condition highest SC during the Day 2 Activation Phase)]; and [(Full Retrieval Control condition highest SC during the Day 3 Activation Phase) – (Full Retrieval Control condition highest SC during the Day 2 Activation Phase)]. It is expected that the Prediction Error condition will show a greater decrease in highest SC from the Day 2 Activation Phase to the Day 3 Activation Phase compared to the Full Retrieval Control condition (i.e., prediction error during the memory activation cue will be necessary to engage memory reconsolidation processes, thus allowing for memory interference on Day 2 and elimination of spontaneous recovery of SC response on Day 3 compared to a memory activation cue without prediction error).
The Sixth ANCOVA

To partially test hypothesis H4, two planned contrasts in the context of the Sixth ANCOVA will be examined: [(Prediction Error condition SC slope during the Day 3 Activation Phase) – (Prediction Error condition SC slope during the Day 2 Activation Phase)]; and [(Full Retrieval Control condition SC slope during the Day 3 Activation Phase) – (Full Retrieval Control condition SC slope during the Day 2 Activation Phase)]. It is expected that the Prediction Error condition will show a greater decrease in SC slope from the Day 2 Activation Phase to the Day 3 Activation Phase compared to the Full Retrieval Control condition (i.e., prediction error during the memory activation cue will be necessary to engage memory reconsolidation processes, thus allowing for memory interference on Day 2 and elimination of spontaneous recovery of SC response on Day 3 compared to a memory activation cue without prediction error).
Within-Condition Analyses

**A.** Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 2 Baseline Phase (condition length = 11; median = 88.62; mean = 91.52; range = 32.81). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 80.00 BPM), so a stability envelope of 15% of the median was used (range = 26.58). Sufficient data (91%) fell within the level stability envelope using all observations suggesting that data across the condition were stable. Relative level change indicated a deterioration of 13.82 BPM across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend direction was accelerating-decelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.

**B.** Data were collected and averaged in 30-second bins for a total of 240 seconds during the Day 2 Activation Phase (condition length = 8; median = 90.27; mean = 90.74; range = 12.19). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 2.06 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 720 seconds during the Day 2 Extinction Phase (condition length = 24; median = 91.85; mean = 94.21; range =
48.85). Sufficient data (96%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 7.38 BPM across the condition. The trend direction was accelerating, and sufficient data (96%) fell within the trend stability envelope, suggesting that the trend was stable.

A2. Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 3 Baseline Phase (condition length = 11; median = 68.20; mean = 71.13; range = 34.63). Sufficient data (91%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 4.50 BPM across the condition. The trend direction was decelerating, and sufficient data (91%) fell within the trend stability envelope suggesting that the trend was stable.

B′. Data were collected and averaged in 30-second bins for a total of 240 seconds during the Day 3 Activation Phase (condition length = 8; median = 66.65; mean = 68.98; range = 8.62). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 5.03 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

Between-Condition Analyses

To examine the effect of the activation task on Control 1’s average HR, changes in average HR data between conditions A1 to B, and between conditions A2 to B′ were first determined.

For A1 to B, PND suggested a 0% impact of condition B on average HR. Absolute level change between conditions indicated an abrupt deterioration of 6.25 BPM. Relative level change
between conditions indicated an improvement of 0.11 BPM. The mean decreased by 0.78 BPM and the median increased by 1.65 BPM. There were no changes in level or trend stability or in trend direction. The range decreased by 20.62 BPM.

For A₂ to B’, PND suggested a 0% impact of condition B’ on average HR. Absolute level change between conditions indicated an abrupt deterioration of 8.60 BPM. Relative level change between conditions indicated a deterioration of 3.94 BPM. The mean decreased by 2.15 BPM and the median decreased by 1.55 BPM. There were no differences in level or trend stability or in trend direction. The range decreased by 26.01 BPM.

Once changes in data between A₁ to B and between A₂ and B’ were determined, these changes were compared. There was no difference in PND. Absolute level change between conditions was 2.35 BPM larger for A₂ to B’, with data deteriorating in both A₁ to B and A₂ to B’. Relative level change between conditions was 3.83 BPM larger for A₂ to B’ with data changing from improving in A₁ to B to deteriorating in A₂ to B’. Means decreased for both A₁ to B and A₂ to B’; the median increased for A₁ to B but decreased for A₂ to B’. There was an increase in Δmean of 1.37 BPM and a decrease in Δmedian of 0.10 BPM for A₂ to B’ compared to A₁ to B. There were no differences in change of level or trend stability or in trend direction. Ranges decreased for both A₁ to B and A₂ to B’. There was an increase in Δrange of 5.39 BPM for A₂ to B’, compared to A₁ to B.
Within-Condition Analyses

**A.** Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 2 Baseline Phase (condition length = 11; median = 17.08; mean = 17.09; range = 11.61). Condition length was greater than or equal to seven, and data were clustered close to the lower half of the scale (i.e., 12.50 μS), so a stability envelope of 25% of the median was used (range = 8.54). Insufficient data (64%) fell within this level stability envelope; therefore, a new stability envelope was calculated using the last five observations of this condition (condition length = 5; median = 22.69; mean = 21.42; range = 5.66). Condition length was then less than seven, so a stability envelope of 25% of the new median was used (range = 11.34). Sufficient data (100%) fell within the level stability envelope using the last five observations suggesting that this subset of the data was stable. Relative level change indicated a deterioration of 3.59 μS across the subset. The subset trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend of the subset was stable.

**B.** Data were collected and averaged in 30-second bins for a total of 240 seconds during the Day 2 Activation Phase (condition length = 8; median = 23.43; mean = 23.58; range = 4.81). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 3.42 μS across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 720 seconds during the Day 2 Extinction Phase (condition length = 24; median = 25.19; mean = 26.06; range = 8.60).
Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 4.27 μS across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

\( A_2 \): Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 3 Baseline Phase (condition length = 11; median = 12.37; mean = 14.19; range = 16.36). Sufficient data (88%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 12.42 μS across the condition. The trend direction was accelerating, and sufficient data (92%) fell within the trend stability envelope suggesting that the trend was stable.

\( B' \): Data were collected and averaged in 30-second bins for a total of 240 seconds during the Day 3 Activation Phase (condition length = 8; median = 19.75; mean = 18.80; range = 13.80). Insufficient data (75%) fell within the level stability envelope suggesting that data were variable. Relative level change indicated an improvement of 9.36 μS across the condition. The trend direction was decelerating, and sufficient data (88%) fell within the trend stability envelope suggesting that the trend was stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Control 1’s highest SC, changes in highest SC data between conditions \( A_1 \) to \( B \), and between conditions \( A_2 \) to \( B' \) were first determined.

For \( A_1 \) to \( B \), PND suggested a 50% impact of condition \( B \) on highest SC. Absolute level change between conditions indicated an abrupt deterioration of 2.26 μS. Relative level change between conditions indicated a deterioration of 2.42 μS. The mean increased by 2.16 μS and the
median increased by 0.74 μS. There were no changes in level or trend stability. The range decreased by 0.85 μS. Trend direction changed from accelerating in the last five observations of A₁, to decelerating in B.

For A₂ to B’, PND suggested a 25% impact of condition B’ on highest SC. Absolute level change between conditions indicated an abrupt deterioration of 8.80 μS. Relative level change between conditions indicated a deterioration of 2.50 μS. The mean increased by 4.61 μS and the median increased by 7.38 μS. The data became variable in B’. There was no change in trend stability. The range decreased by 2.56 μS. Trend direction changed from accelerating in A₂ to decelerating in B’.

Once changes in data between A₁ to B and between A₂ and B’ were determined, these changes were compared. PND was 25% less in A₂ to B’ compared to A₁ to B. Absolute level change between conditions was 6.53 μS larger for A₂ to B’ with data deteriorating in both A₁ to B and A₂ to B’. Relative level change between conditions was 0.08 μS larger for A₂ to B’ with data deteriorating in both A₁ to B and A₂ to B’. Means and medians increased for both A₁ to B and A₂ to B’; there was an increase in Δmean of 2.45 μS and an increase in Δmedian of 6.64 μS for A₂ to B’ compared to A₁ to B. Data remained stable in A₁ to B but became variable in A₂ to B’. Ranges decreased for both A₁ to B and A₂ to B’; there was an increase in Δrange of 1.71 μS for A₂ to B’ compared to A₁ to B. There were no differences in change of trend stability or trend direction.
Subjective Distress (Figure 4)

Within-Condition Analyses

~A. Data were collected every 5 minutes for a total of 30 minutes during the Day 1 Writing Phase (condition length = 7; median = 50.00; mean = 52.86; range = 20.00). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 50.00 units of distress), so a stability envelope of 15% of the median was used (range = 15.00). Sufficient data (86%) fell within the level stability envelope using all observations suggesting that data across the full condition were stable. Relative level change indicated no observed change in subjective distress across the condition. The trend direction was accelerating and sufficient data (86%) fell within the trend stability envelope suggesting that the trend was stable.

B. Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 2 Activation Phase (condition length = 3; median = 78.00; mean = 57.00; range = 87.00). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated a deterioration of 75.00 units of distress across the condition. The trend direction was accelerating; however, insufficient data (67%) fell within the trend stability envelope, suggesting that the trend was variable.

~A'. Data were collected every 5 minutes for a total of 10 minutes during the Day 2 Extinction Phase (condition length = 3; median = 25.00; mean = 28.33; range = 44.00). Insufficient data (67%) fell within the level stability envelope suggesting data were variable. Absolute level change indicated a deterioration of 17.00 units of distress across the condition.
The trend direction was acceleration; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable.

\( B' \). Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 3 Activation Phase (condition length = 3; median = 70.00 mean = 52.33; range = 77.00). Insufficient data (67%) fell within the level stability envelope suggesting data were variable. Absolute level change indicated a deterioration of 65.00 units of distress across the condition. The trend direction was accelerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable.

**Between-Condition Analyses**

To examine the effect of the activation task on Control 1’s subjective distress, changes in SUDS data between conditions \(-A\) to \(B\), and between conditions \(-A'\) to \(B'\), were first determined. The absolute and relative level changes between conditions were not calculated as neither \(-A\) to \(B\) or \(-A'\) to \(B'\) were temporally adjacent.

For \(-A\) to \(B\), PND suggested a 100% impact of condition \(B\) on subjective distress. The mean increased by 4.14 units of distress and the median increased by 28.00 units. Data and trend became variable in condition \(B\). The range increased by 67.00 units. There was no change in trend direction.

For \(-A'\) to \(B'\), PND suggested a 100% impact of condition \(B'\) on subjective distress. The mean increased by 24.00 units of distress and the median increased by 45.00 units. There was no change in level or trend stability or in trend direction. The range increased by 33.00 units.

Once changes in data between \(-A\) to \(B\) and between \(-A'\) to \(B'\) were determined, these changes were compared. There was no difference in PND. Absolute and relative level changes
between conditions were not calculated and therefore could not be compared. Means and medians increased for both A to B and A’ to B’; there was an increase in Δmean of 19.86 units of distress and an increase in Δmedians of 17.00 units of distress for A’ to B’ compared to A to B. There were no differences in change of level or trend stability or in trend direction. Ranges increased for both A to B and A’ to B’; there was a decrease in Δrange of 34.00 units of distress for A’ to B’ compared to A to B.

Posttraumatic Stress Symptoms (Figure 5)

Total Symptoms

Data were collected each day (condition length = 3; median = 39.00; mean = 27.00; range = 42.00). Condition length was less than seven, so a stability envelope of 25% of the median was used (range = 19.50). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated an improvement of 42.00 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that total PTSS improved by 3.00 units prior to the intervention and by 39.00 units following the intervention.

Intrusions Symptoms

Data were collected each day (condition length = 3; median = 6.00; mean = 5.33; range = 10.00). Condition length was less than seven, so a stability envelope of 25% of the median was used (range = 3.00). Insufficient data (33%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated a deterioration of 10.00 units across the
condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that intrusion symptoms improved by 4.00 units prior to the intervention and by 6.00 units following the intervention.

Control 2

Average Heart Rate (Figure 6)

Within-Condition Analyses

**A.** Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 2 Baseline Phase (condition length = 11; median = 163.11; mean = 161.39; range = 17.80). Condition length was greater than or equal to seven, and data were clustered in the high end of the scale (i.e., greater than 120.00 BPM) so a stability envelope of 10% of the median was used (range = 32.62). Sufficient data (100%) fell within the level stability envelope using all observations suggesting that data across the condition were stable. Relative level change indicated an improvement of 2.57 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B.** Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 2 Activation Phase (condition length = 10; median = 142.14; mean = 140.50; range = 28.30). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 2.87 BPM across the condition. The
trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 1890 seconds during the Day 2 Extinction Phase (condition length = 63; median = 159.86; mean = 159.36; range = 32.96). Sufficient data (97%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 3.65 BPM across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**A₂.** Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 3 Baseline Phase (condition length = 11; median = 66.05; mean = 65.46; range = 4.33). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 1.16 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B'.** Data were collected and averaged in 30-second bins for a total of 270 seconds during the Day 3 Activation Phase (condition length = 9; median = 76.71; mean = 75.95; range = 14.11). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 4.82 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.
Between-Condition Analyses

To examine the effect of the activation task on Control 2’s average HR, changes in average HR data between conditions A\textsubscript{1} to B, and between conditions A\textsubscript{2} to B’ were first determined.

For A\textsubscript{1} to B, PND suggested a 90% impact of condition B on average HR. Absolute level change between conditions indicated an abrupt improvement of 10.53 BPM. Relative level change between conditions indicated an improvement of 18.65 BPM. The mean decreased by 20.89 BPM, and the median decreased by 20.97 BPM. There were no changes in level or trend stability or in trend direction. The range increased by 10.50 BPM.

For A\textsubscript{2} to B’, PND suggested a 100% impact of condition B’ on average HR. Absolute level change between conditions indicated an abrupt deterioration of 21.84 BPM. Relative level change between conditions indicated a deterioration of 7.51 BPM. The mean increased by 10.49 BPM, and the median increased by 10.66 BPM. There were no changes in level or trend stability or in trend direction. The range increased by 9.78 BPM.

Once changes in data between A\textsubscript{1} to B and between A\textsubscript{2} and B’ were determined, these changes were compared. PND was 10% more in A\textsubscript{2} to B’ compared to A\textsubscript{1} to B. Absolute level change between conditions was 11.31 BPM larger for A\textsubscript{2} to B’ with data changing from improving in A\textsubscript{1} to B to deteriorating in A\textsubscript{2} to B’. Relative level change between conditions was 11.14 BPM smaller for A\textsubscript{2} to B’ with data changing from improving in A\textsubscript{1} to B to deteriorating in A\textsubscript{2} to B’. Means decreased for A\textsubscript{1} to B and increased for A\textsubscript{2} to B’; the medians increased for both A\textsubscript{1} to B and A\textsubscript{2} to B’. There was a decrease in Δmean of 10.40 BPM and a decrease in Δmedian of 10.31 BPM for A\textsubscript{2} to B’ compared to A\textsubscript{1} to B. There were no differences in change of level or
trend stability, or in trend direction. Ranges increased for both A₁ to B and A₂ to B′; there was a
decrease in Δrange of 0.72 BPM for A₂ to B′ compared to A₁ to B.

**Highest Skin Conductance (Figure 7)**

**Within-Condition Analyses**

**A.** Data were collected and averaged in 30-second bins for a total of 330 seconds during
the Day 2 Baseline Phase (condition length = 11; median = 17.15; mean = 18.59; range = 18.88).
Condition length was greater than or equal to seven, and data were clustered close to the lower
half of the scale (i.e., 12.50 μS) so a stability envelope of 25% of the median was used (range =
8.58). Sufficient data (91%) fell within this level stability envelope using all observations
suggesting that data across the condition were stable. Relative level change indicated a
deterioration of 5.02 μS across the condition. The trend direction was accelerating, and sufficient
data (91%) fell within the trend stability envelope suggesting that the trend was stable.

**B.** Data were collected and averaged in 30-second bins for a total of 300 seconds during
the Day 2 Activation Phase (condition length = 10; median = 31.39; mean = 31.00; range =
7.59). Sufficient data (100%) fell within the level stability envelope suggesting that data were
stable. Relative level change indicated a deterioration of 0.49 μS across the condition. The trend
direction was accelerating, and sufficient data (100%) fell within the trend stability envelope
suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 1890 seconds during
the Day 2 Extinction Phase (condition length = 63; median = 34.20; mean = 34.34; range =
12.07). Sufficient data (89%) fell within the level stability envelope suggesting that data were
stable. Relative level change indicated a deterioration of 1.51 μS across the condition. The trend direction was accelerating, and sufficient data (94%) fell within the trend stability envelope suggesting that the trend was stable.

\( A_2 \) Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 3 Baseline Phase (condition length = 11; median = 20.61; mean = 20.45; range = 3.54). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.65 μS across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

\( B' \) Data were collected and averaged in 30-second bins for a total of 270 seconds during the Day 3 Activation Phase (condition length = 9; median = 24.32; mean = 25.40; range = 12.36). Sufficient data (89%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 2.58 μS across the condition. The trend direction was decelerating, and sufficient data (89%) fell within the trend stability envelope suggesting that the trend was stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Control 2’s highest SC, changes in highest SC data between conditions \( A_1 \) to B and between conditions \( A_2 \) to \( B' \) were first determined.

For \( A_1 \) to B, PND suggested a 10% impact of condition B on highest SC. Absolute level change between conditions indicated an abrupt improvement of 6.87 μS. Relative level change between conditions indicated a deterioration of 10.72 μS. The mean increased by 12.41 μS and
the median increased by 14.24 μS. There were no changes in level or trend stability or in trend direction. The range decreased by 11.29 μS.

For A₂ to B’, PND suggested an 89% impact of condition B’ on highest SC. Absolute level change between conditions indicated an abrupt deterioration of 12.95 μS. Relative level change between conditions indicated a deterioration of 5.97 μS. The mean increased by 4.95 μS and the median increased by 3.71 μS. There were no changes in level or trend stability. The range increased by 8.82 μS. Trend direction changed from accelerating in A₂ to decelerating in B’.

Once changes in data between A₁ to B and between A₂ and B’ were determined, these changes were compared. PND was 79% greater in A₂ to B’ compared to A₁ to B. Absolute level change between conditions was 6.08 μS larger for A₂ to B’ with data changing from improving in A₁ to B to deteriorating in A₂ to B’. Relative level change between conditions was 4.75 μS smaller for A₂ to B’ with data deteriorating in both A₁ to B and A₂ to B’. Means and medians increased for both A₁ to B and A₂ to B’; there was a decrease in Δmean of 7.46 μS and a decrease in Δmedian of 10.53 μS for A₂ to B’ compared to A₁ to B. There were no differences in change of level or trend stability. Ranges decreased for A₁ to B and increased for A₂ to B’; there was a decrease in Δrange of 2.47 μS for A₂ to B’ compared to A₁ to B. Trend direction remained accelerating in A₁ to B and changed from accelerating to decelerating in A₂ to B’.
Subjective Distress (Figure 8)

Within-Condition Analyses

~A. Data were collected every 5 minutes for a total of 70 minutes during the Day 1 Writing Phase (condition length = 15; median = 60.00; mean = 59.67; range = 45.00). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 50.00 units of distress), so a stability envelope of 15% of the median was used (range = 18.00). Insufficient data (60%) fell within this level stability envelope; therefore, a new stability envelope was calculated using the last five observations of this condition (condition length = 5; median = 60.00; mean = 60.00; range = 20.00). Condition length was then less than seven, so a stability envelope of 25% of the new median was used (range = 30.00). Sufficient data (100%) fell within the level stability envelope using the last five observations suggesting that this subset of the data were stable. Relative level change indicated no observed change in subjective distress across the subset. The subset trend direction was accelerating and sufficient data (100%) fell within the trend stability envelope suggesting that the subset trend was stable.

B. Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 2 Activation Phase (condition length = 3; median = 90.00; mean = 68.33; range = 75.00). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated a deterioration of 70.00 units of distress across the condition. The trend direction was accelerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable.

~A’. Data were collected every 5 minutes for a total of 30 minutes during the Day 2 Extinction Phase (condition length = 7; median = 70.00; mean = 64.29; range = 60.00).
Sufficient data (86%) fell within the level stability envelope suggesting data were stable. Relative level change indicated a deterioration of 10.00 units of distress across the condition. The trend direction was accelerating, and sufficient data (86%) fell within the trend stability envelope suggesting that the trend was stable.

**B’**: Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 3 Activation Phase (condition length = 3; median = 20.00 mean = 20.00; range = 20.00). Sufficient data (100%) fell within the level stability envelope suggesting data were stable. Absolute level change indicated a deterioration of 10.00 units of distress across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Control 2’s subjective distress, changes in SUDS data between conditions ~A to B and between conditions ~A’ to B’ were first determined. The absolute and relative level changes between conditions were not calculated, as neither ~A to B or ~A’ to B’ were temporally adjacent.

For ~A to B, PND suggested a 100% impact of condition B on subjective distress. The mean increased by 8.66 units of distress and the median increased by 30.00 units of distress. Data levels and trend became variable in condition B. The range increased by 30.00 units. There was no change in trend direction.

For ~A’ to B’, PND suggested a 33% impact of condition B’ on subjective distress. The mean decreased by 44.29 units of distress and the median decreased by 50.00 units. There was no change in level or trend stability or in trend direction. The range decreased by 40.00 units.
Once changes in data between ~A to B and between ~A’ to B’ were determined, these changes were compared. PND was 67% less in ~A’ to B’ compared to ~A to B. Absolute and relative level changes between conditions were not calculated and therefore could not be compared. Means and medians increased for ~A to B but decreased for ~A’ to B’; there was an increase in Δmean of 35.63 units of distress and an increase in Δmedians of 20 units of distress for ~A’ to B’ compared to ~A to B. Data level and trend became variable in ~A to B and remained stable in ~A’ to B’. Ranges increased for ~A to B but decreased for ~A’ to B’; there was a decrease in Δrange of 10 units of distress for ~A’ to B’ compared to ~A to B. There was no difference in change of trend direction.

Posttraumatic Stress Symptoms (Figure 9)

Total Symptoms

Data were collected each day (condition length = 3; median = 64.00; mean = 63.67; range = 3). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 32.00). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Absolute level change indicated an improvement of 3 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that PTSS improved by 1.00 unit prior to the intervention and by 2.00 units following the intervention.
Intrusions Symptoms

Data were collected each day (condition length = 3; median = 11.00; mean = 13.33; range = 7.00). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 5.50). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated no change across the condition. The trend direction was zero-celerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable. Examination of change in scores pre- and postintervention indicated that intrusion symptoms deteriorated by 7.00 units prior to the intervention and improved by 7.00 units following the intervention.

Intervention 1

Average Heart Rate (Figure 10)

Within-Condition Analyses

A1. Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 2 Baseline Phase (condition length = 11; median = 74.99; mean = 75.39; range = 6.68). Condition length was greater than or equal to seven, and data were clustered near the middle of the scale (i.e., 80.00 BPM), so a stability envelope of 15% of the median was used (range = 22.50). Sufficient data (100%) fell within the level stability envelope using all observations suggesting that data across the condition were stable. Relative level change indicated an improvement of 1.90 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.
B. Data were collected and averaged in 30-second bins for a total of 210 seconds during the Day 2 Activation Phase (condition length = 7; median = 88.22; mean = 88.84; range = 14.60). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 5.69 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

C. Data were collected and averaged in 30-second bins for a total of 1290 seconds during the Day 2 Extinction Phase (condition length = 43; median = 76.19; mean = 76.75; range = 14.15). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 1.91 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

A2. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 3 Baseline Phase (condition length = 10; median = 65.95; mean = 66.62; range = 10.73). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 1.67 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

B’. Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 3 Activation Phase (condition length = 11; median = 69.29; mean = 69.51; range = 17.18). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 2.44 BPM across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle
method. The trend direction was decelerating-accelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 1’s average HR, changes in average HR data between conditions A1 to B and between conditions A2 to B’ were first determined.

For A1 to B, PND suggested a 100% impact of condition B on average HR. Absolute level change between conditions indicated an abrupt deterioration of 13.23 BPM. Relative level change between conditions indicated a deterioration of 16.84 BPM. The mean increased by 13.45 BPM, and the median increased by 13.23 BPM. There were no changes in level or trend stability or in trend direction. The range decreased by 3.42 BPM.

For A2 to B’, PND suggested a 36% impact of condition B’ on average HR. Absolute level change between conditions indicated an abrupt deterioration of 15.53 BPM. Relative level change between conditions indicated a deterioration of 6.62 BPM. The mean increased by 2.89 BPM, and the median increased by 3.34 BPM. There were no changes in level or trend stability or in trend direction. The range increased by 6.45 BPM.

Once changes in data between A1 to B and between A2 and B’ were determined, these changes were compared. PND was 64% less in A2 to B’ compared to A1 to B. Absolute level change between conditions was 2.30 BPM larger for A2 to B’ with data deteriorating in both A1 to B and A2 to B’. Relative level change between conditions was 10.22 BPM smaller for A2 to B’ with data deteriorating in both A1 to B and A2 to B’. Means and medians increased for both A1 to B and A2 to B’; there was a decrease in Δmean of 10.56 BPM and a decrease in Δmedian of 9.89
BPM for A₂ to B’, compared to A₁ to B. There were no differences in change of level or trend stability or in trend direction. Ranges decreased for A₁ to B but increased for A₂ to B’; there was an increase in Δrange of 3.03 BPM for A₂ to B’ compared to A₁ to B.

Highest Skin Conductance (Figure 11)

Within-Condition Analyses

A₁. Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 2 Baseline Phase (condition length = 11; median = 26.53; mean = 27.13; range = 4.69). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 25.00 μS), so a stability envelope of 15% of the median was used (range = 7.96). Sufficient data (100%) fell within this level stability envelope using all observations suggesting that data across the condition were stable. Relative level change indicated a deterioration of 0.04 μS across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend direction was accelerating-decelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.

B. Data were collected and averaged in 30-second bins for a total of 210 seconds during the Day 2 Activation Phase (condition length = 7; median = 35.12; mean = 34.98; range = 4.65). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 1.01 μS across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend
direction was accelerating-decelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.

C. Data were collected and averaged in 30-second bins for a total of 1290 seconds during the Day 2 Extinction Phase (condition length = 43; median = 40.42; mean = 40.31; range = 7.96). Sufficient data (98%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 2.35 μS across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

A₂. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 3 Baseline Phase (condition length = 10; median = 23.85; mean = 23.56; range = 2.85). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.30 μS across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

B'. Data were collected and averaged in 30-second bins for a total of 330 seconds during the Day 3 Activation Phase (condition length = 11; median = 25.70; mean = 26.12; range = 4.56). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.14 μS across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend direction was decelerating-accelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.
Between-Condition Analyses

To examine the effect of the activation task on Intervention 1’s highest SC, changes in highest SC data between conditions A₁ to B and between conditions A₂ to B’ were first determined.

For A₁ to B, PND suggested a 100% impact of condition B on highest SC. Absolute level change between conditions indicated an abrupt deterioration of 6.12 μS. Relative level change between conditions indicated a deterioration of 7.58 μS. The mean increased by 7.85 μS, and the median increased by 8.59 μS. There were no changes in level or trend stability. The range decreased by 0.04 μS. Trend direction changed from decelerating in the end of A₁ (A₁ had multiple paths) to accelerating in the beginning of B (B had multiple paths).

For A₂ to B’, PND suggested an 82% impact of condition B’ on highest SC. Absolute level change between conditions indicated an abrupt deterioration of 5.94 μS. Relative level change between conditions indicated a deterioration of 1.79 μS. The mean increased by 2.56 μS, and the median increased by 1.85 μS. There were no changes in level or trend stability or in trend direction. The range increased by 1.71 μS.

Once changes in data between A₁ to B and between A₂ and B’ were determined, these changes were compared. PND was 18% smaller in A₂ to B’ compared to A₁ to B. Absolute level change between conditions was 0.18 μS smaller for A₂ to B’ with data deteriorating in both A₁ to B and A₂ to B’. Relative level change between conditions was 5.79 μS smaller for A₂ to B’ with data deteriorating in both A₁ to B and A₂ to B’. Means and medians increased for both A₁ to B and A₂ to B’; there was a decrease in Δmean of 5.29 μS and a decrease in Δmedian of 6.74 μS for A₂ to B’ compared to A₁ to B. There were no differences in change of level or trend stability.
Ranges decreased for $A_1$ to $B$ and increased for $A_2$ to $B'$; there was an increase in $\Delta$range of 1.67 $\mu$S for $A_2$ to $B'$ compared to $A_1$ to $B$. Trend direction changed from decelerating to accelerating for $A_1$ to $B$ and remained decelerating for $A_2$ to $B'$.

Subjective Distress (Figure 12)

Within-Condition Analyses

~~A. Data were collected every 5 minutes for a total of 35 minutes during the Day 1 Writing Phase (condition length = 8; median = 50.00; mean = 43.75; range = 80.00). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 50.00 units of distress), so a stability envelope of 15% of the median was used (range = 15.00). Insufficient data (63%) fell within this level stability envelope; therefore, a new stability envelope was calculated using the last five observations of this condition (condition length = 5; median = 60.00; mean = 48.00; range = 80.00). Condition length was then less than seven, so a stability envelope of 25% of the new median was used (range = 30.00). Insufficient data (60%) fell within the level stability envelope using the last five observations; therefore, a new stability envelope was calculated using the last three observations of this condition (condition length = 3; median = 70.00; mean = 50.00; range = 80.00). Condition length was still less than seven, so a stability envelope of 25% of the new median was used (range = 35.00). Insufficient data (67%) fell within the level stability envelope using the last three observations suggesting that this minimal subset of data was variable. Since no subset of data demonstrated level stability, all data within this condition (condition length = 8) and the resulting stability envelope (range = 15.00) will be used for all relevant analyses. Using all data, relative level change indicated a
deterioration of 30.00 units of distress across the condition. The trend direction was accelerating, however insufficient data (63%) fell within the trend stability envelope suggesting that the trend was variable.

**B.** Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 2 Activation Phase (condition length = 3; median = 50.00; mean = 40.00; range = 70.00). Insufficient data (33%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated a deterioration of 50.00 units of distress across the condition. The trend direction was accelerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable.

~~A’.~~ Data were collected every 5 minutes for a total of 20 minutes during the Day 2 Extinction Phase (condition length = 5; median = 40.00; mean = 32.00; range = 60.00). Insufficient data (40%) fell within the level stability envelope; therefore, stability was re-examined using only the last three observations (condition length = 3; median = 40.00; mean = 36.67; range = 50.00). Insufficient data (33%) fell within the level stability envelope suggesting that this minimal subset of data was variable. Since the subset of data did not demonstrate level stability, all data within this condition (condition length = 5) will be used for all relevant analyses. Using all data, relative level change indicated no change in distress across the condition. There appeared to be multiple paths in the data; however, there were not enough observations to create trendlines using the split-middle method. As such, a trendline using all data was created and will be used for all relevant analysis. The trend direction was accelerating, however insufficient data (40%) fell within the trend stability envelope suggesting that the trend was variable.
Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 3 Activation Phase (condition length = 3; median = 60.00 mean = 40.00; range = 60.00). Insufficient data (67%) fell within the level stability envelope suggesting data were variable. Absolute level change indicated a deterioration of 60.00 units of distress across the condition. The trend direction was accelerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable.

**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 1’s subjective distress, changes in SUDS data between conditions ~A to B, and between conditions ~A’ to B’ were first determined. The absolute and relative level changes between conditions were not calculated as neither ~A to B or ~A’ to B’ were temporally adjacent.

For ~A to B, PND suggested a 0% impact of condition B on subjective distress. The mean decreased by 3.75 units of distress and the median decreased by 20.00 units. There were no changes in level or trend stability or in trend direction. The range increased by 10 units.

For ~A’ to B’, PND suggested a 0% impact of condition B’ on subjective distress. The mean increased by 8 units of distress, and the median increased by 20 units. There were no changes in level or trend stability or in trend direction. The range increased by 10 units.

Once changes in data between ~A to B and between ~A’ to B’ were determined, these changes were compared. There was no difference in PND. Absolute and relative level changes between conditions were not calculated and therefore could not be compared. Means and medians decreased for ~A to B and increased for ~A’ to B’; there was an increase in Δmean of 4.25 units of distress and no difference in Δmedian for ~A’ to B’ compared to ~A to B. There
were no differences in change of level or trend stability or in trend direction. Ranges increased for both ~A to B and ~A′ to B′; there was no difference in Δrange for ~A′ to B′ compared to ~A to B.

Posttraumatic Stress Symptoms (Figure 13)

Total Symptoms

Data were collected each day (condition length = 3; median = 22.00; mean = 31.00; range = 27.00). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 11.00). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated an improvement of 17.00 units across the condition. The trend direction was decelerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable. Examination of change in scores pre- and postintervention indicated that PTSS improved by 27.00 units prior to the intervention and did not change following the intervention.

Intrusions Symptoms

Data were collected each day (condition length = 3; median = 4.00; mean = 6.00; range = 12.00). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 3.00). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated an improvement of 12.00 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in
scores pre- and postintervention indicated that intrusion symptoms improved by 9.00 units prior to the intervention and 3.00 units following the intervention.

Intervention 2

Average Heart Rate (Figure 14)

Within-Condition Analyses

A. Data were collected and averaged in 30-second bins for a total of 690 seconds during the Day 2 Baseline Phase (condition length = 23; median = 88.59; mean = 89.02; range = 11.08). Condition length was greater than or equal to seven, and data were clustered near the middle of the scale (i.e., 80.00 BPM), so a stability envelope of 15% of the median was used (range = 26.58). Sufficient data (100%) fell within the level stability envelope using all observations suggesting that data across the condition were stable. Relative level change indicated a deterioration of 2.20 BPM across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

B. Data were collected and averaged in 30-second bins for a total of 180 seconds during the Day 2 Activation Phase (condition length = 6; median = 97.02; mean = 94.72; range = 13.00). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 0.52 BPM across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend direction was accelerating-decelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.
C. Data were collected and averaged in 30-second bins for a total of 1350 seconds during the Day 2 Extinction Phase (condition length = 45; median = 86.33; mean = 86.88; range = 18.35). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 1.11 BPM across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

A2. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 3 Baseline Phase (condition length = 10; median = 81.18; mean = 81.39; range = 4.09). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.52 BPM across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

B′. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 3 Activation Phase (condition length = 10; median = 88.61; mean = 88.40; range = 5.97). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 1.50 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 2’s average HR, changes in average HR data between conditions A1 to B, and between conditions A2 to B′ were first determined.
For A₁ to B, PND suggested a 67% impact of condition B on average HR. Absolute level change between conditions indicated an abrupt improvement of 4.87 BPM. Relative level change between conditions indicated a deterioration of 7.04 BPM. The mean increased by 5.70 BPM and the median increased by 8.43 BPM. There were no differences in level or trend stability or in trend direction. The range increased by 1.92 BPM.

For A₂ to B’, PND suggested a 100% impact of condition B’ on average HR. Absolute level change between conditions indicated an abrupt deterioration of 9.29 BPM. Relative level change between conditions indicated a deterioration of 6.98 BPM. The mean increased by 7.01 BPM, and the median increased by 7.43 BPM. There were no differences in level or trend stability. The range increased by 1.88 BPM. Trend direction changed from accelerating in A₂ to decelerating in B’.

Once changes in data between A₁ to B and between A₂ to B’ were determined, these changes were compared. PND was 33% greater in A₂ to B’ compared to A₁ to B. Absolute level change between conditions was 4.42 BPM larger for A₂ to B’ with data improving in A₁ to B and deteriorating in A₂ to B’. Relative level change between conditions was 0.06 BPM smaller for A₂ to B’ with data deteriorating in both A₁ to B and A₂ to B’. Means and medians increased for both A₁ to B and A₂ to B’; there was an increase in Δmean of 1.31 BPM and a decrease in Δmedian of 1.00 BPM for A₂ to B’ compared to A₁ to B. There were no differences in change of level or trend stability. Ranges increased for both A₁ to B and A₂ to B’; there was a decrease in Δrange of 0.04 BPM for A₂ to B’ compared to A₁ to B. Trend direction remained accelerating in A₁ to B and changed from accelerating to decelerating in A₂ to B’.
Within-Condition Analyses

**A.** Data were collected and averaged in 30-second bins for a total of 690 seconds during the Day 2 Baseline Phase (condition length = 23; median = 33.01; mean = 33.59; range = 16.70). Condition length was greater than or equal to seven, and data were clustered close to the high end of the scale (i.e., 37.50 μS), so a stability envelope of 10% of the median was used (range = 6.30). Insufficient data (70%) fell within this level stability envelope using all observations; therefore, a new stability envelope was calculated using the last five observations of this condition (condition length = 5; median = 37.97; mean = 36.43; range = 12.35). Condition length was then less than seven, so a stability envelope of 25% of the new median was used (range = 18.98). Sufficient data (100%) fell within the level stability envelope using the last five observations suggesting that this subset of data was stable. Relative level change indicated a deterioration of 9.90 μS across the subset. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B.** Data were collected and averaged in 30-second bins for a total of 180 seconds during the Day 2 Activation Phase (condition length = 6; median = 33.17; mean = 33.54; range = 12.09). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 10.05 μS across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 1350 seconds during the Day 2 Extinction Phase (condition length = 45; median = 35.71; mean = 35.47; range =
30.93). Insufficient data (73%) fell within this level stability envelope using all observations; therefore, level stability was re-examined using the last five observations of this condition (condition length = 5; median = 47.41; mean = 48.73; range = 7.93). Sufficient data (100%) fell within the level stability envelope using the last five observations suggesting that this subset of data was stable. Relative level change indicated an improvement of 2.24 μS across the subset. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

A2. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 3 Baseline Phase (condition length = 10; median = 29.43; mean = 29.37; range = 10.34). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.55 μS across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend direction was accelerating-decelerating, and sufficient data (100% and 100% respectively) fell within the trend stability envelopes suggesting that the trends were stable.

B'. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 3 Activation Phase (condition length = 10; median = 25.18; mean = 26.29; range = 11.13). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 4.76 μS across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.
**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 2’s highest SC, changes in highest SC data between conditions A₁ to B and between conditions A₂ to B’ were first determined.

For A₁ to B, PND suggested a 33% impact of condition B on highest SC. Absolute level change between conditions indicated an abrupt improvement of 3.24 μS. Relative level change between conditions indicated an improvement of 1.14 μS. The mean decreased by 2.89 μS, and the median decreased by 4.80 μS. There were no differences in level or trend stability. The range decreased by 0.26 μS. Trend direction changed from accelerating in the last five observations of A₁ to decelerating in B.

For A₂ to B’, PND suggested a 20% impact of condition B’ on highest SC. Absolute level change between conditions indicated an abrupt deterioration of 4.81 μS. Relative level change between conditions indicated an improvement of 1.41 μS. The mean decreased by 3.08 μS, and the median decreased by 4.25 μS. There were no differences in level or trend stability or in trend direction. The range increased by 0.79 μS.

Once changes in data between A₁ to B and between A₂ and B’ were determined, these changes were compared. PND was 13% smaller in A₂ to B’ compared to A₁ to B. Absolute level change between conditions was 1.57 μS greater for A₂ to B’, with data changing from improving in A₁ to B to deteriorating in A₂ to B’. Relative level change between conditions was 0.27 μS greater for A₂ to B’ with data improving in both A₁ to B and A₂ to B’. Means and medians increased for both A₁ to B and A₂ to B’; there was an increase in Δmean of 0.19 μS and a decrease in Δmedian of 0.55 μS for A₂ to B’, compared to A₁ to B. There were no differences in
change of level or trend stability. Ranges decreased for $A_1$ to $B$ and increased for $A_2$ to $B'$; there was an increase in $\Delta$range of 0.53 $\mu$S for $A_2$ to $B'$ compared to $A_1$ to $B$. Trend direction changed from accelerating to deceleration in $A_1$ to $B$, and remained decelerating in $A_2$ to $B'$.

Subjective Distress (Figure 16)

Within-Condition Analyses

~A. Data were collected every 5 minutes for a total of 55 minutes during the Day 1 Writing Phase (condition length = 12; median = 60.00; mean = 58.75; range = 45.00). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 50.00 units of distress), so a stability envelope of 15% of the median was used (range = 18.00). Insufficient data (67%) fell within this level stability envelope; therefore, a new stability envelope was calculated using the last five observations of this condition (condition length = 5; median = 60.00; mean = 64.00; range = 15.00). Condition length was then less than seven, so a stability envelope of 25% of the new median was used (range = 30.00). Sufficient data (100%) fell within the level stability envelope using the last five observations suggesting that this subset of data was stable. Relative level change indicated an improvement of 7.50 units of distress across the subset. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

B. Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 2 Activation Phase (condition length = 3; median = 50.00; mean = 43.33; range = 20.00). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Absolute level change indicated a deterioration of 20.00 units of
distress across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

\( \sim A' \). Data were collected every 5 minutes for a total of 20 minutes during the Day 2 Extinction Phase (condition length = 5; median = 50.00; mean = 50.00; range = 55.00). Sufficient data (80%) fell within the level stability envelope suggesting that the data were stable. Relative level change indicated a deterioration of 7.50 units of distress across the condition. There appeared to be multiple paths in the data; however, there were not enough observations to create trendlines using the split-middle method. As such, a trendline using all data was created and will be used for all relevant analysis. The trend direction was accelerating; however, insufficient data (60%) fell within the trend stability envelope suggesting that the trend was variable.

\( B' \). Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 3 Activation Phase (condition length = 3; median = 40.00 mean = 38.33; range = 45.00). Insufficient data (67%) fell within the level stability envelope suggesting data were variable. Absolute level change indicated a deterioration of 25.00 units of distress across the condition. The trend direction was accelerating; however, insufficient data (67%) fell within the trend stability envelope suggesting that the trend was variable.

**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 2’s subjective distress, changes in SUDS data between conditions \( \sim A \) to B and between conditions \( \sim A' \) to B’ were first determined. The absolute and relative level changes between conditions were not calculated as neither \( \sim A \) to B or \( \sim A' \) to B’ were temporally adjacent.
For ~A to B, PND suggested a 100% impact of condition B on subjective distress. The mean decreased by 20.67 units of distress, and the median decreased by 10.00 units. There were no differences in level or trend stability. The range increased by 10 units. Trend direction changed from decelerating in the last five observations of ~A to accelerating in B.

For ~A′ to B′, PND suggested a 0% impact of condition B′ on subjective distress. The mean decreased by 11.67 units of distress, and the median decreased by 10.00 units. The data became variable in condition B′; there were no differences in trend stability or direction. The range decreased by 10.00 units.

Once changes in data between ~A to B and between ~A′ to B′ were determined, these changes were compared. PND decreased by 100% for A′ to B′. Absolute and relative level changes between conditions were not calculated and therefore could not be compared. Means and medians decreased for both ~A to B and ~A′ to B′; There was a decrease in Δmean of 9.00 units of distress and no difference in Δmedian for A′ to B′ compared to A to B. Data remained stable in ~A to B and became variable in ~A′ to B′. There were no differences in change of trend stability. Ranges increased for ~A to B but decreased for ~A′ to B′; there was no difference in Δrange. Trend direction changed from decelerating to accelerating in ~A to B and remained accelerating in ~A′ to B′.

Posttraumatic Stress Symptoms (Figure 17)

Total Symptoms

Data were collected each day (condition length = 3; median = 50.00; mean = 55.67; range = 19.00). Condition length was then less than seven, so a stability envelope of 25% of the
median was used (range = 25.00). Sufficient data (100%) fell within the level stability envelope, suggesting that data were stable. Absolute level change indicated an improvement of 19.00 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that PTSS improved by 18.00 units prior to the intervention and by 1.00 unit following the intervention.

**Intrusions Symptoms**

Data were collected each day (condition length = 3; median = 9.00; mean = 10.67; range = 5.00). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 4.50). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated an improvement of 5.00 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that intrusion symptoms improved by 5.00 units prior to the intervention and did not change following the intervention.

**Intervention 3**

**Average Heart Rate (Figure 18)**

**Within-Condition Analyses**

$A_t$. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 2 Baseline Phase (condition length = 10; median = 83.82; mean = 84.28; range = 22.09).
Condition length was greater than or equal to seven, and data were clustered near the middle of the scale (i.e., 80.00 BPM), so a stability envelope of 15% of the median was used (range = 25.14). Sufficient data (100%) fell within the level stability envelope using all observations suggesting that data across the condition were stable. Relative level change indicated an improvement of 4.72 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B.** Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 2 Activation Phase (condition length = 10; median = 82.64; mean = 82.93; range = 5.57). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 2.99 BPM across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 1380 seconds during the Day 2 Extinction Phase (condition length = 46; median = 84.64; mean = 84.81; range = 17.82). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 3.94 BPM across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**A2.** Data were collected and averaged in 30-second bins for a total of 360 seconds during the Day 3 Baseline Phase (condition length = 12; median = 86.60; mean = 88.18; range = 22.00). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 1.37 BPM across the condition. The trend
direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B’.** Data were collected and averaged in 30-second bins for a total of 420 seconds during the Day 3 Activation Phase (condition length = 14; median = 85.23; mean = 86.10; range = 9.60). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.52 BPM across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 3’s average HR, changes in average HR data between conditions A₁ to B, and between conditions A₂ to B’ were first determined.

For A₁ to B, PND suggested a 0% impact of condition B on average HR. Absolute level change between conditions indicated an abrupt improvement of 0.35 BPM. Relative level change between conditions indicated a deterioration of 0.33 BPM. The mean decreased by 1.35 BPM, and the median decreased by 1.28 BPM. There were no differences in level or trend stability. The range decreased by 16.52 BPM. Trend direction changed from decelerating in A₁ to accelerating in B.

For A₂ to B’, PND suggested a 0% impact of condition B’ on average HR. Absolute level change between conditions indicated an abrupt improvement of 21.76 BPM. Relative level change between conditions indicated an improvement of 2.16 BPM. The mean decreased by 2.08 BPM, and the median decreased by 1.37 BPM. There were no differences in level or trend
stability. The range decreased by 12.40 BPM. Trend direction changed from accelerating in A₂ to decelerating in B'.

Once changes in data between A₁ to B and between A₂ and B' were determined, these changes were compared. There was no difference in PND between A₁ to B and A₂ to B'. Absolute level change between conditions was 21.41 BPM larger for A₂ to B' with data improving in both A₁ to B and A₂ to B'. Relative level change between conditions was 1.83 BPM larger for A₂ to B' with data deteriorating in A₁ to B and improving in A₂ to B'. Means and medians decreased for both A₁ to B and A₂ to B'; there was an increase in Δmean of 0.73 BPM and an increase in Δmedian of 0.09 BPM for A₂ to B' compared to A₁ to B. There was no difference in change of level or trend stability. Ranges decreased for both A₁ to B and A₂ to B'; there was a decrease in Δrange of 4.12 BPM for A₂ to B' compared to A₁ to B. Trend direction changed from decelerating to accelerating in A₁ to B, but changed from accelerating to decelerating in A₂ to B'.

**Highest Skin Conductance (Figure 19)**

**Within-Condition Analyses**

A₁. Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 2 Baseline Phase (condition length = 10; median = 22.35; mean = 23.88; range = 13.66). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 25.00 μS), so a stability envelope of 15% of the median was used (range = 6.70). Sufficient data (80%) fell within this level stability envelope using all observations suggesting that the data across the condition were stable. Relative level change indicated a
deterioration of 3.56 μS across the condition. There appeared to be multiple paths in the data, so trendlines were created using the split-middle method. The trend direction was decelerating-accelerating, and sufficient data (100% and 80% respectively) fell within the trend stability envelopes suggesting that the trends were stable.

**B.** Data were collected and averaged in 30-second bins for a total of 300 seconds during the Day 2 Activation Phase (condition length = 10; median = 33.03; mean = 33.36; range = 4.42). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 1.13 μS across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**C.** Data were collected and averaged in 30-second bins for a total of 1380 seconds during the Day 2 Extinction Phase (condition length = 43; median = 37.29; mean = 36.93; range = 10.85). Sufficient data (81%) fell within this level stability envelope suggesting that the data were stable. Relative level change indicated an improvement of 1.23 μS across the subset. The trend direction was decelerating, and sufficient data (84%) fell within the trend stability envelope suggesting that the trend was stable.

**A2.** Data were collected and averaged in 30-second bins for a total of 360 seconds during the Day 3 Baseline Phase (condition length = 12; median = 36.25; mean = 36.78; range = 9.33). Insufficient data (75%) fell within the level stability envelope; therefore, stability was re-examined using only the last five observations (condition length = 5; median = 37.85; mean = 39.19; range = 4.44). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated an improvement of 0.50 μS across the
subset of data. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B’**. Data were collected and averaged in 30-second bins for a total of 420 seconds during the Day 3 Activation Phase (condition length = 14; median = 37.27; mean = 36.81; range = 4.01). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Relative level change indicated a deterioration of 0.92 µS across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**Between-Condition Analyses**

To examine the effect of the activation task on Intervention 3’s highest SC, changes in highest SC data between conditions A₁ to B, and between conditions A₂ to B’ were first determined.

For A₁ to B, PND suggested a 60% impact of condition B on highest SC. Absolute level change between conditions indicated an abrupt improvement of 1.23 µS. Relative level change between conditions indicated a deterioration of 9.46 µS. The mean increased by 9.48 µS, and the median increased by 10.68 µS. There were no differences in level or trend stability. The range decreased by 9.24 µS. Trend direction changed from accelerating in the end of A₁ (A₁ had multiple paths) to decelerating in B.

For A₂ to B’, PND suggested a 0% impact of condition B’ on highest SC. Absolute level change between conditions indicated an abrupt improvement of 2.41 µS. Relative level change between conditions indicated an improvement of 1.71 µS. The mean increased by 0.03 µS, and
the median increased by 1.02 μS. There were no differences in level or trend stability or in trend direction. The range decreased by 0.43 μS.

Once changes in data between \( A_1 \) to \( B \) and between \( A_2 \) and \( B' \) were determined, these changes were compared. PND was 60% smaller in \( A_2 \) to \( B' \) compared to \( A_1 \) to \( B \). Absolute level change between conditions was 1.18 μS greater for \( A_2 \) to \( B' \) with data improving in both \( A_1 \) to \( B \) and \( A_2 \) to \( B' \). Relative level change between conditions was 7.75 μS less for \( A_2 \) to \( B' \) with data deteriorating in \( A_1 \) to \( B \) and improving in \( A_2 \) to \( B' \). Means and medians increased for both \( A_1 \) to \( B \) and \( A_2 \) to \( B' \); there was a decrease in Δmean of 9.45 μS and a decrease in Δmedian of 9.66 μS for \( A_2 \) to \( B' \) compared to \( A_1 \) to \( B \). There were no differences in change of level or trend stability. Ranges decreased for both \( A_1 \) to \( B \) and \( A_2 \) to \( B' \); there was a decrease in Δrange of 8.81 μS for \( A_2 \) to \( B' \) compared to \( A_1 \) to \( B \). Trend direction changed from accelerating to decelerating in \( A_1 \) to \( B \) and remained decelerating in \( A_2 \) to \( B' \).

Subjective Distress (Figure 20)

Within-Condition Analyses

\(~\text{A.}\) Data were collected every 5 minutes for a total of 40 minutes during the Day 1 Writing Phase (condition length = 9; median = 55.00; mean = 56.67; range = 20.00). Condition length was greater than or equal to seven, and data were clustered close to the middle of the scale (i.e., 50.00 units of distress), so a stability envelope of 15% of the median was used (range = 16.50). Insufficient data (78%) fell within this level stability envelope; therefore, a new stability envelope was calculated using the last five observations of this condition (condition length = 5; median = 60.00; mean = 60.80; range = 12.00). Condition length was then less than seven, so a
stability envelope of 25% of the new median was used (range = 30.00). Sufficient data (100%) fell within the level stability envelope using the last five observations suggesting that this subset of data was stable. Relative level change indicated a deterioration of 9.50 units of distress across the subset. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B.** Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 2 Activation Phase (condition length = 3; median = 72.00; mean = 61.33; range = 38.00). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated a deterioration of 35.00 units of distress across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

~**A′.** Data were collected every 5 minutes for a total of 20 minutes during the Day 2 Extinction Phase (condition length = 5; median = 61.00; mean = 61.60; range = 17.00). Sufficient data (100%) fell within the level stability envelope suggesting that the data were stable. Relative level change indicated a deterioration of 6.50 units of distress across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.

**B′.** Data were collected before and after the activation task and retrospectively for the highest during the task during the Day 3 Activation Phase (condition length = 3; median = 56.00 mean = 48.00; range = 38.00). Insufficient data (67%) fell within the level stability envelope suggesting data were variable. Absolute level change indicated a deterioration of 31.00 units of distress across the condition. The trend direction was accelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable.
Between-Condition Analyses

To examine the effect of the activation task on Intervention 3’s subjective distress, changes in SUDS data between conditions ~A to B, and between conditions ~A’ to B’ were first determined. The absolute and relative level changes between conditions were not calculated as neither ~A to B or ~A’ to B’ were temporally adjacent.

For ~A to B, PND suggested a 100% impact of condition B on subjective distress. The mean increased by 0.53 units of distress, and the median increased by 12.00 units. Data became variable in condition B; there were no differences in trend stability or direction. The range increased by 26.00 units.

For ~A’ to B’, PND suggested a 33% impact of condition B’ on subjective distress. The mean decreased by 13.60 units of distress, and the median decreased by 5.00 units. Data became variable in condition B’; there were no differences in trend stability or direction. The range increased by 21.00 units.

Once changes in data between ~A to B and between ~A’ to B’ were determined, these changes were compared. PND decreased by 67% for ~A’ to B’. Absolute and relative level changes between conditions were not calculated and therefore could not be compared. Means and medians increased for ~A to B and decreased for ~A’ to B’; there was an increase in Δmean of 13.07 units of distress and a decrease in Δmedian of 7.00 units for ~A’ to B’ compared to ~A to B. There were no differences in change of level or trend stability or in trend direction. Ranges increased for both ~A to B and ~A’ to B’; there was a decrease in Δrange of 5.00 units for ~A’ to B’ compared to ~A to B.
Posttraumatic Stress Symptoms (Figure 21)

Total Symptoms

Data were collected each day (condition length = 3; median = 32.00; mean = 35.67; range = 17.00). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 16.00). Sufficient data (100%) fell within the level stability envelope suggesting that data were stable. Absolute level change indicated an improvement of 17.00 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that PTSS improved by 14.00 units prior to the intervention and by 3.00 units following the intervention.

Intrusions Symptoms

Data were collected each day (condition length = 3; median = 10.00; mean = 7.67; range = 7.00). Condition length was then less than seven, so a stability envelope of 25% of the median was used (range = 5.00). Insufficient data (67%) fell within the level stability envelope suggesting that data were variable. Absolute level change indicated an improvement of 7.00 units across the condition. The trend direction was decelerating, and sufficient data (100%) fell within the trend stability envelope suggesting that the trend was stable. Examination of change in scores pre- and postintervention indicated that intrusion symptoms did not change prior to the intervention and improved by 7 units following the intervention.
APPENDIX C

PROPOSED THIRD ITERATION OF A BEHAVIORAL MEMORY RECONSOLIDATION
FOR THE TREATMENT OF POSTTRAUMATIC STRESS SYMPTOMS
Issues to Address

The results of the current (second) iteration of the treatment protocol suggest several changes that should be implemented in subsequent iterations. The primary issues to be addressed are: 1) the restructuring of the Activation Phase; 2) the expansion of baseline data collection for PTSS and intrusion symptoms; and 3) the restructuring of the eligibility criteria and tracking measures.

Issue 1

Although there may be evidence of some effect of the intervention, this evidence is weak and inconsistent, thus precluding any clinical utility of the protocol as designed. It is possible that the activation task was insufficient to produce reliable memory activation and destabilization, and these possible failures should be addressed in the next study iteration. The first failure is that the “dose” of the activation task may have not been sufficient to destabilize a trauma memory. There are two methods by which the dose may be increased.

First, the activation task will need to be time-limited to reduce the likelihood of engaging extinction mechanisms and preventing reconsolidation processes. I propose that the activation cue be limited to a maximum of a 30-second clip of the trauma narrative with the clip containing only up to 30-seconds leading up to the “most distressing” part of the narrative. A 30-second audio clip of a trauma narrative has been successfully used before as an activation cue during a study of pharmacological memory reconsolidation interference (Brunet et al., 2008). Ideally, this will increase the chances of destabilizing the memory and allowing reconsolidation processes to initiate.
Second, the Activation Cue should include a more salient prediction error. As is, the “prediction error” is simply a sudden stop to the audio recording right at the “most distressing” part. Although this stop may represent a prediction error in the participant’s expectations for the audio recording, it is possible that it does not represent a prediction error in the expectations for the memory itself, as the participant may continue to think about what happened next in the event and thus fulfil their expectations. Said differently, a sudden stop to the recording is not an unexpected turn for events of the memory; it is simply an interruption. Drawing from the memory rescripting literature (e.g., Arntz & Weertman, 1999; Salter, 2014; Smucker, 2005; Smucker et al., 1995) may allow for a more salient prediction error that is respectful of the participant’s experiences. Thus, I propose that the 30-second activation cue used to destabilize the memory stop at the most distressing part and then the experimenter say, “I would now like you to imagine that the event happened differently. Imagine that…” and describe a brief change to the next part of the memory that is individualized. For example, a participant with a motor vehicle accident as their index event would listen to the 30 seconds leading up to the most distressing part (e.g., the moment their vehicle was hit), then the experimenter would say, “I would now like you to imagine that the event happened differently. Imagine the other vehicle stopping just in time and you driving home safely.” This method may provide a more salient prediction error by forcing the participants to imagine an ending to their index event that is entirely unexpected, thus increasing the chances of memory destabilization.

Issue 2

Evidence from the current study suggests that any potential effect of the intervention on PTSS or intrusion symptoms may have been obscured by natural recovery and/or natural
fluctuations in symptoms. Furthermore, it is possible that a single session of a written exposure may be sufficient for some participants to experience symptom decreases. Rapid improvements in distress are sometimes observed for individuals following disclosure experiences (e.g., Hemenover, 2003), and the writing task was derived from a current treatment protocol (WET; Sloan et al., 2012). As such, the writing task itself could be considered an active therapeutic session. To account for these concerns, I propose that the participants complete their written narratives on Day 1, then complete weekly symptom-tracking measures until data stability is achieved. Only when data stability has been established should participants return to the lab for the intervention. Participants who see symptom remission to below accepted cutoffs (i.e., a total PCL-5 score of 31; Bovin et al., 2015) should be dismissed from the study.

**Issue 3**

Individual differences may have affected outcomes and will need to be addressed in future study iterations. The best example of the effect of these differences can be seen in the case of Intervention 2. Intervention 2’s pattern of results was unlike any other participant, yet was more similar to participants in the Control condition than to those in the Intervention condition. There are several possible reasons for these findings including sleep deprivation, possible poor distress tolerance, and possible relatively increased avoidance behavior. Considering Intervention 2’s results were most similar to Control 2 and both were the only participants with symptoms in the “severe” range, it is also possible that high-symptom severity may interfere with the study protocol, possibly through heightened avoidance. Further, Intervention 3’s unexpected HR outcomes may be attributable to relatively higher anticipatory anxiety, as Intervention 3’s results were consistent with literature suggesting that HR may be especially
sensitive to anticipatory anxiety and worry (Hofmann et al., 2005; Thayer & Brosschot, 2008), unlike SC (Delgado et al., 2009; Wilhelm et al., 2001). Finally, Control 2 was the only participant to experience an increase in intrusions following the intervention. It is possible that this increase in symptoms was due to their unique index event in which they were both a victim and a perpetrator.

The easiest method for controlling for these potentially important individual differences is to exclude participants who exhibit the hypothesized confounds. This exclusion can be done for participants with sleep deprivation and perpetration histories. However, excluding participants high in avoidance, intolerance of distress, and anticipatory anxiety would diminish the external validity of the study past the point of clinical utility. For example, avoidance behavior is central to many theories of PTSS (for a review, see Brewin & Holmes, 2003); excluding participants high in avoidance would potentially exclude the majority of individuals who would need or seek treatment. Instead, measures of avoidance, distress tolerance, and anticipatory anxiety/worry should be included in the weekly questionnaire packets in the next study iteration. In this way, possible relationships between individual differences and treatment outcomes can be more thoroughly examined.

Overview of Iteration 3 Protocol

Three conditions should be utilized in this study: Condition 1 will follow the retrieval-extinction paradigm by including only extinction training during the reconsolidation window; Condition 2 will follow the visuospatial interference paradigm by including only playing Tetris during the reconsolidation window; and Condition 3 will utilize the combined paradigm used in the second iteration of this study by including both extinction training and playing Tetris during
the reconsolidation window. There will be no other differences between conditions. The use of these three conditions will allow for the examination of the effectiveness of each possible paradigm for targeting memory reconsolidation processes, which may inform later iterations of study design. Three participants should be recruited per condition and data should be collected for all conditions according to the following method.

The Writing Day of the protocol will be mostly the same as Day 1 in the original dissertation proposal, including the Questionnaire Phase and Writing Phase. The only difference should be that the participants be asked for their SUDS every 5 minutes during the Writing Phase. Further, they should draw a line in their narrative to indicate when they were asked. This change to the protocol will allow for identification of the “most distressing part” of the narrative without examination of emotion and self-referential words. It is possible that participants high in avoidance would use fewer of such words during the most distressing part. Using SUDS during this phase may allow researchers to more accurately target the section of the memory that engenders the most distress.

Following the Writing Day but prior to Intervention Day 1, the narrative created during the Writing Phase will be read and recorded by a research assistant (the full narrative recording). The “most distressing” section will be determined using participant SUDS ratings from the Writing Day, and a second audio file will be recorded containing only up to 30 seconds leading up to this section as well as the participant’s individualized memory rescripting instructions (the Activation Cue).

Between the Writing Day and Intervention Day 1 (Pre-I1 – Pre-In), participants should complete the questionnaire packet weekly at home until PTSS and intrusion symptoms are shown to be stable. Those who experience a decrease in symptoms to below 31 after the Writing
Day will be dismissed from the study and new participants recruited in their place. Once stability is established, participants should return to the lab for Intervention Day 1.

Intervention Day 1 of the protocol will be similar to what was described for Day 2 of the original dissertation proposal, including the Questionnaire Phase, Habituation Phase, Baseline Phase, Activation Phase, and the Distraction Phase and/or Extinction Phase (depending on condition, as described above). However, Participant 2 and Participant 3 will take the place of the Control condition by listening to their full narrative recording during the Activation Phase. Participant 1 will take the place of the Intervention Condition by listening to their Activation Cue during the Activation Phase. All other procedures will remain the same between participants.

Intervention Day 2 of the protocol will be the same Intervention Day 1; however, Participant 1 and Participant 3 will listen to their full narrative recording during the Activation Phase and Participant 2 will listen to their Activation Cue.

Intervention Day 3 of the protocol will be the same as Intervention Day 1 and 2, except Participant 1 and Participant 2 will listen to their full narrative recording during the Activation Phase and Participant 3 will listen to their Activation Cue.

Intervention Day 4 will be the same as Intervention Day 1, 2, and 3 except all participants will listen to their full narrative recording during the Activation Phase.

The staggered single-case design proposed above allows for several observations. First, by establishing PTSS and intrusion data stability prior to Intervention Day 1, any effect of the intervention or control on participants can be observed. Second, by having Participant 1 receive their Activation Cue on Intervention Day 1, follow-up observations for their reconsolidation intervention can be examined over the following three weeks (Intervention Day 2 – Intervention Day 4). Third, by having Participant 3 receive their Activation Cue on Intervention Day 3,
can be obtained for the two weeks prior to their reconsolidation intervention (Intervention Day 1 – Intervention Day 2), in which Participant 3 will receive two weeks of the control exposure to their trauma memory without the prediction error, and follow-up data can be collected on Intervention Day 4. This data will allow for comparisons of outcomes following the reconsolidation intervention versus following exposure without prediction error both within and across participants, thus testing the hypothesis that prediction error is necessary for the reconsolidation paradigm. Finally, Participant 2 will have one week of data collection with exposure alone (Intervention Day 1), then two weeks of follow-up (Intervention Day 2 – Day 3), further allowing for examination of the necessity of the prediction error and stability of outcomes. Therefore, the hypotheses of the original proposal will be restructured as:

1) A decreased SUDS response during activation will be observed following the prediction error intervention compared to SUDS response during activation following the intervention without a prediction error.

2) A decreased psychophysiological response during activation will be observed following the prediction error intervention compared to the psychophysiological response during activation following the intervention without a prediction error.

3) Decreased PTSS will be observed following the prediction error intervention compared to PTSS following the intervention without a prediction error.

4) Decreased intrusion symptoms will be observed following the prediction error intervention compared to intrusion symptoms following the intervention without a prediction error.