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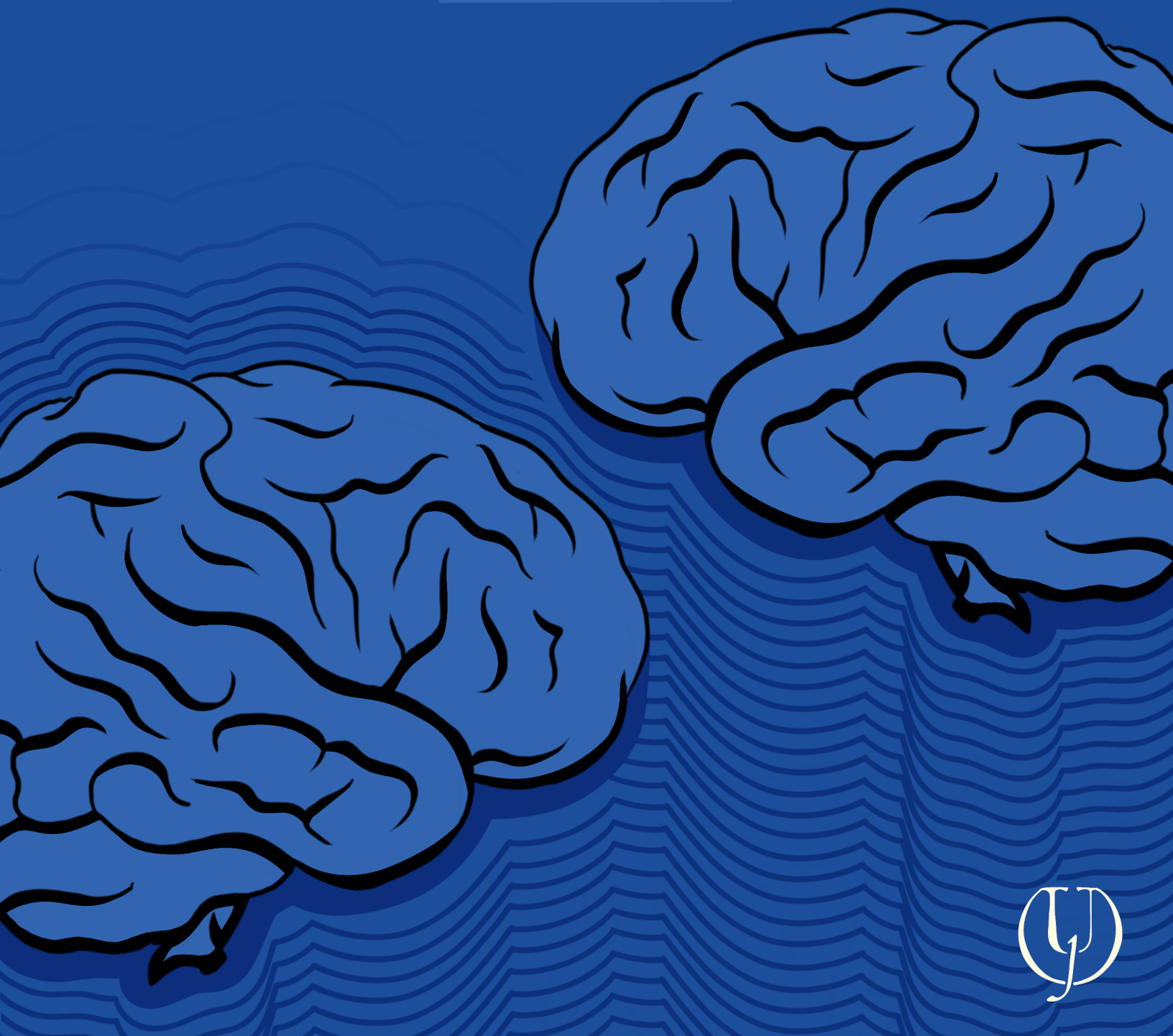


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Special thanks to our founders and past members, Dr. Aaron P. Blaisdell, Dylan Sarnowski and the rest of the University of California, Los Angeles, Department of Psychology, and all of the faculty, staff, and graduate students who have supported us throughout the years.

NOTE FROM THE EDITORS-IN-CHIEF

Dear readers,

It is with great pride and pleasure that we present to you the ninth volume of The Undergraduate Research Journal of Psychology at UCLA. We are continuously amazed and blown away by the resilience of the psychological and neuroscience undergraduate research community. Despite the ongoing COVID-19 pandemic and the ongoing injustices our society continues to face, student researchers around the world prevailed in providing us with the insightful manuscripts for this year's publication.

As always, our journal would not be the same without the consistent hard work, passion, and dedication our team members put forth, all of which went above and beyond this year in their respective contributions. We have immense appreciation for our Submissions and Workshops team, who worked hard to collect and process the over a hundred submissions we received this year in addition to providing our staff with invigorating workshops. Our Marketing and Finance Team was extremely advantageous in their efforts to provide our journal with a growing online presence, and our successful fundraising campaigns, as well as playing a key role in finalizing our journal from front to back. The Editing Team was highly commendable in their dedication to the rigorous editing process they undertake to review and refine articles, which is evident in the high quality of our manuscripts. We would also like to thank our wonderful graduate student mentors, who provided steadfast mentorship, invaluable knowledge, and continued support to our staff throughout the academic year. We want to thank our faculty advisor, Professor Blaisdell, without whom this would not have been possible.

Lastly, we want to thank our authors – their diligence and hard work in revising their manuscript led to the culmination of this publication. It is their love, and the love all our submissions' authors have, for research that makes us say with utmost confidence that the future of psychology and neuroscience research is bright. Their contribution to the field of psychology is a foundation for future work that is to come and an inspiration to all students to continue to ask questions. We look forward to continuing to capture that in our annual publications as well as being a long-lasting resource to uplift undergraduate research and provide them with a safe space to share their valuable contributions for years to come.

Sincerely,

Stephanie Rivas-Lara and Talia Leano

Editors-in-Chief

PREFACE



Dillon H. Murphy, M.A.
Doctoral Candidate, Cognitive Psychology
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It is my pleasure to write the preface for The Undergraduate Research Journal of Psychology (URJP) at UCLA. This journal, run by UCLA undergraduates, represents a premier outlet for undergraduate psychology research. Although it can sometimes be frustrating, publishing research in peer-reviewed journals is the cornerstone of scientific development.

Before empirical research is published, it should undergo peer review (the evaluation of research by others). The peer-review process helps refine scientific work by ensuring sound methodology, appropriate statistical techniques, and clarity. Peer review is also an essential learning opportunity for young researchers to think critically—reviewers must evaluate the quality of the design, the validity of the measures, as well as the impact and relevance of the work. The URJP team has demonstrated an exemplary ability to evaluate and improve the research displayed in this year's issue.

As beneficial as the peer review process is, the system can be difficult and may even discourage some researchers from attempting to publish their work. However, if research is not published, how can anyone benefit from it? Without journals to publish our work, other researchers and society as a whole would never learn of new discoveries, bringing scientific advancement to a halt. For example, if we are unable to share our findings, other researchers may investigate issues that have already been studied rather than building on the most up-to-date information about a topic. When each successive psychology paper builds on previously published work, we learn more and more about the mind, brain, and behavior. Thus, when we learn something new, it is pivotal that this work is shared with the world.

Despite the many benefits of making research available to the public, publishing research papers can be an arduous process. It involves not only writing the first draft, but also revising it over and over again, submitting it to a journal, dealing with potentially harsh reviews, and revising the manuscript again to make the findings clearer, a process that often takes many months or even years. But if you persevere, the moment when your paper is accepted is one of the best feelings in your career. As such, I would like to congratulate all the authors and their collaborators for their hard work and perseverance as well as the amazing URJP team supervising the peer review process. Because of the dedication of the authors and the entire team at URJP, we all benefit from the fascinating work published in this year's issue.

Without further ado, please proceed with the 2022 issue of URJP to learn about indicators of post-traumatic stress disorder, potential eye-movement-based therapy for post-traumatic stress disorder, predictors of adolescent disruptive and/or delinquent behaviors, and risk factors for the development of postpartum psychosis. Each paper sheds new light on different topics within psychology and was written by undergraduate scholars from across the country. The four new papers in this ninth volume of the URJP represent only a fraction of the incredible undergraduate research occurring across the globe. I encourage all passionate researchers to continue conducting research and to pursue the publication of their excellent work in peer-reviewed journals like URJP.

Sincerely,

A handwritten signature in black ink that reads "Dillon Murphy". The script is fluid and cursive.

Dillon Murphy
July 2022

Katie Hurman, BA

University of Oxford

My name is Katie Hurman and I graduated from the University of Oxford in 2021 with a first-class BA in Experimental Psychology. During my second and third years at Oxford, I wrote numerous research reports and conducted my own research study on the effects of mindfulness on social exclusion. During my third year, I also assisted in the Attention, Brain and Cognitive development laboratory, assisting with the development of eye tracking technology and a study looking at attention in dyslexia. Throughout my degree, I developed a strong interest in Clinical Psychology, with a particular focus on PTSD, anxiety and depression. After university I worked as a research assistant on a PTSD study, and I am now working as an assistant psychologist for the NHS in an anxiety and depression team.



Was there a particular experience that sparked your research interests?

Having studied the barriers to mental health treatment, I identified acceptability, efficacy and accessibility as important barriers. Therefore, I was interested in researching alternative methods to improve acceptability and accessibility to treatment, ensuring that this is not at the cost of efficacy. I am also motivated by the idea of contributing to the optimisation of mental health treatments.

Who has been the most influential person in your life?

My family have all greatly influenced me in my life. My parents are both very supportive and always encouraged me to do what makes me happy. They did their best to support me every step of the way. My grandad also taught

me to make the most out of life and he inspired me with his compassionate personality to help other people make the most out of theirs.

What is your greatest accomplishment?

My greatest accomplishment is getting into Oxford University and witnessing all my hard work pay off. Being able to study under some of the leaders in the psychological field was inspiring and helped me to develop my passion for research and mental health.

Where do you see yourself in 10 years?

In 10 years time, I hope to be a qualified Clinical Psychologist. With this status, I hope to be able to develop and test new protocols to increase accessibility to mental health treatment and work to increase their efficacy. I would like to specialise in anxiety.

Investigating Whether Eye Movements are Necessary for Eye Movement Desensitisation and Reprocessing (EMDR)

Katie Hurman

University of Oxford

Eye movement desensitisation and reprocessing (EMDR) is a first-choice therapy for PTSD which uniquely involves eye movements to abate the intrusive symptoms and negative appraisals that maintain PTSD. However, there has been significant controversy surrounding the incorporation of eye movements and whether they can be replaced by alternative types of stimulation or alternative tasks that engage dual attention. This is important in order to optimise EMDR and to increase its accessibility. Therefore, a literature review was conducted of studies investigating the effects of eye movements, auditory stimulation, tactile stimulation, and alternative dual tasks on memories within EMDR. While the results seem promising, the lack of clarity in this domain is apparent from the methodological limitations in studies assessing the efficacy of eye movements and the gap in the research assessing alternative stimulation and tasks. This demonstrates important avenues for future research to advance EMDR therapy for people with PTSD.

Keywords: EMDR; Eye movements; Stimulation; Dual tasks

Experiencing a traumatic event catalyses the development of posttraumatic stress disorder (PTSD), a mental health disorder associated with intrusive symptoms related to an event, avoidance behaviours, alterations in cognition and mood, and hyperarousal (American Psychiatric Association [APA], 2013). Many people are likely to encounter a traumatic event, such as an assault, a severe accident, or a natural disaster, during their lifetime (Kessler et al., 1995) and evidence suggests that nearly a third of those who are exposed to a traumatic event will develop PTSD (Committee on Treatment of Posttraumatic Stress Disorder & Institute of Medicine, 2008). According to Carriere (2014), there are around 500 million people facing PTSD worldwide and therefore may be burdened with debilitating symptoms, such as flashbacks, nightmares, emotional numbness, hypervigilance, sleeping problems, and concentration difficulties. This, and the chronic course PTSD takes, demonstrates the necessity of finding appropriate treatments. Accessing treatment has proven difficult (Davis et al., 2009) and outcomes are not optimal, with high heterogeneity amongst study outcomes (Cuijpers et al., 2020). In order to optimise treatments, it is necessary to understand PTSD and the mechanisms by which treatments target individual aspects of the disorder.

Many psychological processes are disturbed by PTSD, but unlike other disorders, the disturbance of memory representations appears to be the most central and unique aspect. One cognitive model formulated by Ehlers and Clark (2000)

proposes that negative appraisals, among other factors, maintain PTSD. For example, people may overgeneralize aspects from an event, making normal experiences seem more dangerous than they really are, resulting in fear and avoidance of them. An example of this may be avoiding swimming after nearly drowning because there is a heightened unrealistic expectation of nearly drowning again. People with PTSD may also negatively appraise their own actions and responses to the event, such as attributing emotional numbing (i.e., blocking emotional responses) to feeling “dead inside.” In addition to negative appraisals, the Ehlers and Clark model suggests that the nature of the trauma memory maintains PTSD, given that trauma memories are fragmented and not sufficiently integrated into the autobiographical memory system, where memories of past experiences are stored. This inhibits memory elaboration and leads to a disjointed narrative. It has also been suggested that fragmented memories include increased sensory components (Hopper & van der Kolk, 2001). Eye movement desensitisation and reprocessing (EMDR) treats both negative appraisals and traumatic memories. This treatment works to desensitise the trauma memory and reintegrate it into the autobiographical memory system, as well as install positive cognitions.

The EMDR protocol (Shapiro, 2017) describes eight stages of treatment. The first stage involves aggregating and analyzing the patient’s history to identify the trauma memory. This is followed by preparation for treatment (stage two). In the third

stage, the therapist will elucidate specific thoughts, emotions, and physiological sensations which the patient has associated with the trauma memory. The fourth stage involves desensitization, where the patient will recall the memory while engaging in bilateral stimulation, most commonly eye movements, until the memory is no longer deemed uncomfortable. The fifth stage is the resource development and installation phase, where a pre-determined positive cognition is linked to the original memory through bilateral stimulation. The therapist then proceeds to focus on physiological sensations and debriefs the patient. At the beginning of the following session, a re-evaluation is conducted to determine if the effects were maintained and to identify targets that need to be addressed. These stages are outlined further in Figure 1 (see appendix).

EMDR has proven to be an effective treatment in meta-analyses (Cuijpers et al., 2020) and has been recommended as a first-choice therapy for PTSD by the World Health Organisation (WHO; 2013) and the National Institute for Health and Care Excellence (NICE; 2018). However, evidence for a precise mechanism underpinning the efficacy of EMDR is inconclusive. A systematic review by Landin-Romero et al. (2018) detailed the evidence for a potential mechanism of EMDR, finding reasonable support for the working memory hypothesis; notably, it may work alongside other mechanisms. The working memory hypothesis suggests that the dual attention task of performing bilateral eye movements while retrieving the traumatic memory exhausts the working memory system (Gunter & Bodner, 2008). The working memory system is composed of a central executive, which is involved in high-order cognitive functions, the visuospatial sketchpad, and the phonological loop, which processes and stores visual and spatial information, and auditory information, respectively (Baddeley, 1986). The working memory system is known to have limited capacity, and thus, performing a demanding task depletes the capacity to hold information in the system. For example, conjuring up the image of the traumatic memory places it within the visuospatial sketchpad component of the working memory system. Performing bilateral eye movements requires using other processing resources which reduces the efficiency of working memory and depletes the resources available for maintaining and elaborating upon the image. This results in a reduction in the vividness and emotionality of the image. The resulting visuospatial image is then consolidated into long-term memory with decreased vividness and emotionality attached to it (Kavanagh et al., 2001). It is important to note that this is not a definitive account of the mechanism of action, but a likely one, and further research is required to underpin the exact mechanism.

In addition to this debate, there is discourse as to whether eye movements are a necessary component of EMDR. This has been investigated in contradictory meta-analyses (Davidson & Parker, 2001; Lee & Cuijpers, 2013) and ongoing studies. Clinical evidence suggests that eye movements are often disliked by patients who can find them tiring and distracting (van den Hout et al., 2012).

Such evidence highlights the importance of determining whether eye movements are necessary for EMDR efficacy. Patients with intellectual disabilities, have been shown to have a higher likelihood of experiencing a traumatic event (Hulbert-Williams et al., 2014). Unfortunately, they have also been shown to find eye movements particularly difficult (Barol & Seubert, 2010). Furthermore, people with impairments to the motor and oculomotor system may struggle to perform eye movements. For example, a meta-analysis has shown impaired tracking of moving targets in individuals with autism (Johnson et al., 2016). Therefore, increasing the accessibility of EMDR could benefit from removing eye movements or use alternative forms of stimulation. The EMDR protocol (Shapiro, 2017) states that eye movements can be replaced by bilateral auditory or tactile stimulation. Bilateral auditory stimulation involves sounds alternating between the left and right side of the head, whilst bilateral tactile stimulation involves tapping the left and right hands in alternation. However, without strong evidence establishing them as efficacious, psychologists are cautious to use forms of stimulation other than eye movements (Unwin et al., 2019). Additionally, studies have demonstrated the efficacy of alternative dual tasks (Houben et al., 2020), which involve performing a task, such as counting, during memory recall. These have been shown to evoke similar effects to eye movements.

In this paper, a literature review is presented of studies assessing the efficacy of eye movements, as well as auditory and tactile stimulation and alternative dual tasks. The goal of this review is to assist in optimising EMDR as a first-line treatment for PTSD. This is achieved by providing an overview of the empirical studies published to date, identifying clear gaps in the literature, and assessing methodological issues across studies which limit any strong conclusions from being drawn. Therefore, this review allows clear future directions to be formulated that will advance and improve our knowledge of EMDR.

Eye Movements in Stage 4 of EMDR: The Desensitisation Phase

Treatment studies involve the full EMDR procedure either with or without eye movements. Various studies have assessed the efficacy of eye movements in the desensitization phase of EMDR (Stage 4), which is intended to desensitize the trauma memory. This often involves measuring the intensity of distress, given that the Subjective Units of Distress (SUD) scale (Wolpe, 1969) is used in EMDR as an outcome measure, and is used to determine the point at which Stage 4 is complete. Laboratory studies typically assess the effects of desensitization by evaluating vividness of the trauma memory, which refers to the strength and clarity of the mental image, and emotionality, which refers to the emotional distress associated with the memory. Reducing vividness and emotionality associated with the trauma memory is an aim of PTSD therapies. Regarding the necessity of eye movements for desensitization, however, there are mixed results, with some studies finding that eye movements are efficacious and others finding success

without eye movements. This section will discuss these varied results as well as the methodological differences and limitations which hinder strong conclusions from being made.

Studies Suggesting Eye Movements are Efficacious

The general consensus from treatment studies is that eye movements are efficacious in EMDR. For example, Lee and Drummond (2008) found that when focusing on a negative autobiographical memory with non-clinical participants, eye movements in Stage 4 of EMDR elicited a significantly greater reduction in distress than no eye movements, measured using SUD scores. Even stronger evidence came from Schubert et al. (2011), which found the same results with non-clinical participants but with the use of trained EMDR therapists. Most importantly, similar results were found for individuals with panic disorder (Feske & Goldstein, 1997) and patients with PTSD (Shapiro, 1989; Wilson et al., 1996; van den Hout et al., 2012) using both EMDR trained therapists and the EMDR manual. These studies offer good evidence to support the efficacy of eye movements.

The majority of laboratory studies demonstrated greater reductions in the vividness and/or emotionality of memories as a result of eye movements compared to no eye movements. These effects were found for various types of memories, including mental images of aversive pictures (Andrade et al., 1997), aversive mental images of a film (Leer et al., 2013), craving-induced memories (Markus et al., 2016), feared images of future events (Engelhard et al., 2010), and even sexual fantasies (Bartels et al., 2018). However, negative autobiographical memories of healthy participants have the greatest predictive validity of those involved in EMDR for patients with PTSD, as they incorporate the emotional and personal associations of trauma memories. The majority of studies using these memories demonstrated greater reductions in vividness and/or emotionality following eye movements in comparison to recall only. Such reductions have even been found when comparing eye movements to a stationary eyes condition with moving visual images to replicate the visual images seen during eye movements, ruling background movement out as a confounding variable (Onderdonk & van den Hout, 2016). Evidence in favor of the inclusion of eye movements has been gained from laboratory studies conducted with patients experiencing PTSD (Lilley et al., 2009; Matthijssen et al., 2019) or intrusive images as well (Homer & Deepprose, 2018). This lends further credence to the importance of eye movements.

Intrusions refer to involuntary thoughts or images and, given that they are a core feature of PTSD (Ehlers & Clark, 2000), it is important to assess whether eye movements can reduce them. Only two studies were identified that focused on this aspect. Van Schie et al. (2019) evaluated the effects of recall with eye movements compared to no task on the number of intrusions associated with a trauma film of a murder in a nightclub. Their first experiment showed no effect, but their second experiment increased the duration of the eye movements, resulting in

lower numbers of intrusions. However, when including a recall only condition, their third experiment showed no association between eye movements and intrusions. Patel and McDowall (2016) also assessed the effects of eye movements on negative memories, finding that fast eye movements led to fewer intrusions. The current evidence suggests that eye movements during recall may reduce intrusions; however, given that only two studies have assessed the impact of eye movements, further studies are warranted.

Studies Suggesting Eye Movements are Not Necessary in EMDR

Some treatment studies have demonstrated that EMDR is as efficacious at reducing distress without eye movements as it is with eye movements, suggesting that they might not be strictly necessary. This may be due to the fact that control conditions typically involve eye fixation, which can also be deemed a dual attention task when recalling a trauma memory. For example, Renfrey and Spates (1994) demonstrated that distress and heart reactivity decreased for patients with PTSD as a result of standard EMDR involving eye movements, and to a similar extent in a variant where eyes were fixated. Similar results were obtained from other studies using the same outcome measures (Boudewyns & Hyer, 1996; Dunn et al., 1996) and from studies using blood pressure as an outcome measure (Deville et al., 1998). Furthermore, a study looking at reductions in symptomatology and intrusions found no significant difference between conditions (Pitman et al., 1996). This suggests that eye movements may not yield any benefit in EMDR, as eye fixation elicits similar effects. A more recent randomized controlled trial involving a large sample of patients with PTSD ($n = 139$) has shown symptom reduction and remission rates to be comparable following eye movements and eye fixation in EMDR (Sack et al., 2016). Notably, this study used trained and experienced practitioners of EMDR and may have involved stronger therapeutic allegiances (McLeod, 2009) which could have increased the efficacy of experimental conditions. Further studies with trained therapists that measure these allegiances would be useful to determine whether this has an effect. Overall, while these studies suggest that eye fixation may be equally as effective as eye movements, there are a larger number of studies finding a greater effect of eye movements, and thus the results must be interpreted with caution.

Notably, some laboratory studies argue against the use of eye movements in EMDR due to finding no reductions in vividness or emotionality. However, two of the studies showing no change in vividness and emotionality involved either word-image pairs (van Schie, et al., 2015) or neutral autobiographical memories (Littel, Remijn, et al., 2017), which are unlikely to stimulate sufficient arousal required for reductions in vividness (Littel, Kenemans, et al., 2017). Furthermore, while Thomaes et al. (2016) found no change following eye movements, their study was underpowered, and they did find a correlation between neurobiological changes and emotional changes. Similarly, Kearns

and Engelhard (2015) found no effects of eye movements on self-reports of vividness and emotionality, but they did find a reduction in heart rate. This demonstrates the benefit of using objective and subjective measures, as it prevents incorrect conclusions from being made.

Long-term effects of eye movements in Stage 4 of EMDR

Inconsistencies have arisen among studies that include follow-up tests, suggesting that the benefits of eye movements within EMDR may be short-lived. For example, van Veen et al. (2020) assessed the effects the following day, finding that vividness and emotionality increased for those in the eye movement condition. The authors suggest that this could be due to eye movements acting as safety behaviours during exposure, where safety is misattributed to the eye movements and therefore without the eye movements the perceived threat is enhanced. Greater reductions in vividness and emotionality following eye movements have been found to persist at a one-week follow-up (Gunter & Bodner, 2008). However, two studies found that reductions in vividness and emotionality returned to baseline at a one-week follow up, with one involving healthy participants (Kavanagh et al., 2001) and the other involving PTSD patients (Lilley et al., 2009). These studies suggest that while eye movements may have an immediate beneficial effect on memory, it is unclear whether the effects persist. It is important to note that studies typically involve one session of EMDR, which is unlikely able to leave lasting changes to the nature of the trauma memory. Typically, EMDR involves 6 to 12 sessions.

Strengths and Limitations of Studies

There are various limitations in the treatment studies discussed that hinder strong conclusions from being made. For example, some were not restricted to patients with PTSD, either measuring distress in non-clinical populations (Dunn et al., 1996; Lee & Drummond, 2008; Schubert et al., 2011) or focusing on patients with other disorders, such as public-speaking anxiety (Foley & Spates, 1995; Carrigan & Levis, 1999) or panic disorder (Feske & Goldstein, 1997). It may be that the outcomes are different for different populations. Others did not follow the full EMDR protocol (Boudewyns & Hyer, 1996), did not use independent ratings (Devilly et al., 1998), or lacked trained therapists (Renfrey & Spates, 1994). Therefore, these studies do not conclusively provide evidence against the necessity of eye movements in a full session of EMDR administered by trained therapists following a therapy manual for patients with PTSD. Furthermore, it is unclear whether the modality of the trauma memory was consistent between studies, or even between participants. It is important that future studies note whether the memories were primarily visual, as EMDR may have different effects for different types of memory modality (e.g., auditory).

Nonetheless, the majority of the studies supporting the use of eye movements are laboratory studies. These prevent confounding variables that may be found

in treatment studies from explaining any benefits found with eye movements during EMDR, such as therapeutic allegiance which refers to the relationship between the therapist and patient, cognitive restructuring which refers to changes in thoughts, beliefs and evaluations (Clark, 2013) and even the background movement associated with eye movements. Notably, the majority of these studies do not involve patients with PTSD and therefore the results may not be generalizable to this population. While it is important that future studies address these limitations, overall these studies suggest that eye movements are useful in EMDR.

Eye Movements in Stage 5 of EMDR: The Resource Development and Installation (RDI) Phase

The purpose of the RDI phase is to install a positive cognition, and the protocol states that this process involves eye movements. This is based on the rationale that eye movements help to facilitate adaptive associations (Shapiro, 2001). However, research has suggested that eye movements are not essential during this phase.

In one study, eye movements were found to increase the vividness and strength of positive memories after a one-minute processing period, but they were not significantly more effective than eye fixation (Keller et al., 2014). Additional research has found no significant change in emotionality or belief of positive personal verbal material following eye movements, compared to no eye movements, in non-clinical undergraduate students (Matthijssen & van den Hout, 2016a). A subsequent study involving PTSD patients also involved recalling positive personality traits (e.g., persistence) with or without eye movements, following targeting a traumatic memory with EMDR (Matthijssen & van den Hout, 2016b). Again, no benefits of eye movements were found.

One study did find an effect of eye movements, but this effect was not significant. Hornsvelt et al. (2011) assessed the effects of eye movements on positive memories with healthy participants, demonstrating a reduction in vividness, emotionality, and strength when compared to when no eye movements were involved. These results led to conclusions that eye movements may not be useful in the RDI phase.

Strengths and Limitations of Studies

Although there is no clear evidence to support the use of eye movements in the RDI phase, the largely non-clinical populations used in studies (Hornsvelt et al., 2011; Keller et al., 2014; Matthijssen & van den Hout, 2016b) rather than individuals with PTSD means that the results should not be generalised to this population and the possibility that eye movements are clinically useful in the RDI phase should not be excluded. Notably, Matthijssen and van den Hout (2016a) did use a PTSD population, although the generalisability of their results is limited by the small sample size ($n = 36$).

In addition, methodological problems such as the brief nature of the eye movements (Matthijssen & van den Hout,

2016b) limit conclusions that can be drawn, given that a single set of eye movements lasting only 20 seconds may be insufficient to induce an effect. Furthermore, the nature of the material used in studies (i.e., personality traits; Matthijssen & van den Hout, 2016a; Matthijssen & van den Hout, 2016b) may have prevented a significant outcome, as personality traits may not easily change over time. Therefore, the results should not be generalised to specific positive autobiographical memories.

It is also important to assess the efficacy of the whole of the RDI procedure. Hornsveld et al. (2011) only involved steps 3 (resource development), 4 (checking the resource), and 5 (resource installation) of the RDI procedure, which were administered by untrained experimenters, and thus may miss out critical components for establishing an effect. For example, step 6 involves strengthening the resource. It is important to identify the mechanism underpinning the RDI phase to determine whether eye movements are useful and until then, studies should not dismantle the RDI procedure to investigate the effect of eye movements as they may miss out important components for establishing an effect.

The lack of conclusive support for the use of eye movements combined with methodological limitations concerning objective demonstrates the necessity for further research to be conducted in order to determine whether eye movements are necessary in this phase. This should involve the administration of the full RDI phase of EMDR with clinical patients, with the addition and absence of eye movements. It is critical that papers with singular findings are not used to prove that eye movements are not necessary without conducting systematic reviews to consider the full array of findings.

Investigating Alternatives to Eye Movements

Auditory Stimulation

Auditory stimulation can be used in EMDR as an alternative form of bilateral stimulation by presenting patients with sounds, such as beeps, alternating between the right and left ear. This is often done using headphones. If the working memory hypothesis is correct, it would suggest that auditory stimulation works by taxing the phonological loop and thereby reduces the vividness and emotionality of memories during recall. Given that auditory stimulation can be preferred by patients (de Jongh et al., 2013; van den Hout et al., 2012), it is important to assess its effectiveness at reducing vividness and emotionality, and how it compares to eye movements. However, few studies have investigated this.

Caution for the use of auditory stimulation in EMDR comes from evidence demonstrating its inferiority to eye movements. For example, van den Hout, Engelhard, Rijkeboer, et al. (2011) compared the effects of eye movements, alternating bilateral beeps, and no stimulation on the recall of negative autobiographical memories by students. They demonstrated that the beeps reduced the vividness of the memory relative to no task, but eye movements resulted in a significantly greater reduction in vividness. Van

den Hout et al. (2012) found similar results for patients with PTSD, showing that eye movements were more effective at reducing vividness and emotionality of aversive memories than tones. This study was limited by its small sample size ($n = 12$), but the results were reinforced by de Jongh et al. (2013), showing eye movements were more efficacious for 32 patients with PTSD.

Only one study has looked at the effects of auditory stimulation on distress, showing positive, yet limited, results (Servan-Schreiber et al., 2006). In this study, the full EMDR procedure was administered to patients with PTSD by trained therapists, replacing eye movements with auditory and tactile stimulation. Patients rated their current level of disturbance at different time points, as it occurs in EMDR sessions. They found that the stimulation led to reductions in distress, regardless of whether it was alternating, intermittent, or continuous. However, the outcomes were not compared to a control group, and so the effects cannot be directly attributed to the auditory and tactile stimulation (time could be a contributing factor).

Overall, there seems to be insufficient evidence to advocate the use of bilateral auditory stimulation in EMDR as there is indication that eye movements are more effective. In line with the working memory hypothesis, this may be due to the primarily visual nature of memories in studies, as it has been suggested that it may be beneficial to align the mode of dual attention with the modality of the memory to achieve optimum results (Lilley et al., 2009). Nonetheless, the fact that auditory stimulation can also be effective suggests that eye movements may not be necessary for EMDR. This is an area that is severely under-researched and thus it is vital that further research is conducted to assess the efficacy of bilateral auditory stimulation.

Tactile Stimulation

Tactile stimulation is another alternative method of bilateral stimulation used in EMDR, which typically involves the therapist tapping the patient's left and right hands in alternation. Indeed, evidence has suggested that EMDR using tactile stimulation is effective at reducing the post-traumatic symptoms of clinical patients (Bourgou et al., 2019). It may be that this works by taxing the spatial component of the visuospatial sketchpad in working memory during recall to desensitize the memory.

Four studies assessed the effects of bilateral tactile stimulation that was administered externally to healthy participants, finding that it has positive effects on memories compared to no stimulation. As mentioned earlier, Servan-Schreiber et al. (2006) found reductions in subjective distress following EMDR involving auditory stimulation or tactile stimulation with small vibrating devices on the palms. However, they did not separate the effects from each type of stimulation. Furthermore, in a study by Reichel et al. (2020), participants were to read and imagine the content of affective scripts to induce positive and negative emotions. They found greater reductions in distress and emotional reactivity towards negative scripts following bilateral tactile stimulation, where rhythmically

changing vibration signals were applied to the palms. Bilateral tactile stimulation was also found to increase arousal for positive scripts, demonstrating its effects for the RDI phase. However, this study did not involve personal memories as it would in EMDR treatment. A neurological study has also supported the use of tactile stimulation in the RDI phase. Amano and Toichi (2016) used near-infrared spectroscopy to show that alternating bilateral tactile stimulation with a vibration machine increased activation of the right superior temporal sulcus, which is associated with pleasant memory representation. This suggests that the stimulation increased accessibility of memories. They also found reduced activity in the prefrontal cortex, which is associated with emotion regulation. Therefore, it may be that tactile stimulation regulates emotions associated with memories. However, while these studies suggest that tactile stimulation may be effective in EMDR, they do not directly compare the outcomes of EMDR with tactile stimulation to those with eye movements.

There is limited evidence comparing the efficacy of tactile stimulation with eye movements. One experimental study involving healthy participants demonstrated enhanced recall following alternating bilateral tactile stimulation when compared to simultaneous bilateral tactile stimulation, showing similar previous outcomes to eye movements while not directly comparing the results (Nieuwenhuis et al., 2013). As with auditory stimulation, there is a clear gap in the literature comparing tactile stimulation with eye movements in EMDR, and as such it is unclear whether tactile stimulation is equally as efficacious as eye movements. Given that none of the studies discussed involved patients with PTSD, there is a clear need to utilise this population to identify whether tactile stimulation is effective in EMDR as a treatment for PTSD.

Alternative Dual Tasks

Alternative dual tasks, which involve performing an alternative task during memory recall, such as counting or playing Tetris, have also been found to lead to memory desensitization. This supports the notion that the effects on memory are linked to tasks requiring dual attention and that eye movements are only one of many such tasks. This may be due to the fact that these tasks tax working memory during memory recall and desensitize the memory.

Visuospatial tasks are a type of alternative dual task that involve vision and space and engage the visuospatial component of the working memory system. Eye movements may be classified as visuospatial tasks, but alternative examples include shape sorting and the computer game Tetris. Indeed, shape sorting has been found to reduce vividness and emotionality of the memory of a virtual reality game (Cuperus et al., 2016), and playing the computer game Tetris has been found to reduce the vividness and emotionality of autobiographical memories (Engelhard et al., 2010), including memories from the 9/11 terrorist attack witnessed during childhood (Rackham & Lau-Zhu, 2021). This may have been due to the positively induced mood caused by the game, so future studies should compare positive and negative affect before

and after the experimental condition to ensure that Tetris works in the same way as eye movements to desensitise the memory. Nonetheless, a study by Tsai and McNally (2014) suggested that a positive task has greater effects on memories than a neutral or negative task. This suggests that it would be useful for studies to assess the effects of tasks with positive emotional valence to determine whether they are superior to the neutral task of eye movements.

Furthermore, studies have demonstrated the efficacy of performing alternative non-visuospatial tasks to auditory and tactile bilateral stimulation, such as mental arithmetic, whilst recalling a memory. One study demonstrated a reduction in vividness and emotionality of a stressful news event when simultaneously engaging in a subtraction task during recall (Engelhard et al., 2011). However, stronger evidence comes from studies involving personal memories. In a study by van den Hout et al. (2010), participants engaged in a subtraction task while holding a negative memory in mind and results showed that both simple and complex subtraction tasks decreased the vividness and emotionality of the memory. Even listening to counting, which differs from bilateral auditory stimulation as the stimulation is not bilateral, has been shown to reduce the vividness of unpleasant autobiographical memories (Kristjánsdóttir & Lee, 2011). This is likely due to taxation of the phonological loop. Non-visuospatial tasks, such as auditory shadowing where participants listen to a voice say 'ta' repeatedly (Gunter & Bodner, 2008) and attentional breathing where participants are instructed to focus their attention on their breath (Slofstra et al., 2016; van den Hout, Engelhard, Beetsma, et al., 2011) have also been shown to reduce the vividness and emotionality of autobiographical memories when performed during memory recall. Therefore, it seems that other types of non-visuospatial tasks that tax working memory during memory recall could potentially replace eye movements in EMDR.

Nonetheless, four studies have suggested that eye movements are more effective than non-visuospatial tasks (Andrade et al., 1997; Homer et al., 2016; Kristjánsdóttir & Lee, 2011; van den Hout et al., 2001). For example, Homer et al. (2016) demonstrated that for participants with public speaking anxiety, who experience feared images, engaging in a visuospatial letter identification task led to significantly greater reductions in vividness of a feared image than a task involving responding to spoken target letters; however, this visuospatial task did involve alternating bilateral eye movements. Further research should remove this aspect in order to demonstrate the effect of dual attention, rather than the alternating bilateral nature of eye movements. Studies involving tapping, where participants rhythmically tap their fingers on a table, have found mixed results, with one suggesting that tapping is not effective at all (van den Hout et al., 2001), another suggesting that tapping is as efficacious as eye movements (Merckelbach et al., 1994), and another suggesting that tapping is less efficacious to eye movements (Andrade et al., 1997). This may be linked to the working memory hypothesis, where taxing the spatial component of the visuospatial sketchpad is not as effective as taxing the visual

and spatial components, as it occurs with eye movements.

A further three studies have rejected the efficacy of alternative tasks (Matthijssen et al., 2017; Mertens et al., 2019; van Schie et al., 2019). Matthijssen et al. (2017) compared the effects of eye movements with a counting task for patients with PTSD, showing that although emotionality was reduced, the results did not differ from those of a control condition involving visual fixation. The same results were found in a counting task with healthy participants when recalling a novel traumatic memory witnessed in a film (van Schie et al., 2019). However, a study by Littel and van Schie (2019) found that reductions in vividness and unpleasantness became significantly greater as the complexity of the counting task increases. Therefore, the prior null results may be due to the counting task being too simple.

Overall, these studies generally seem to advocate the use of alternative dual tasks. The evidence suggesting that alternative tasks are as efficacious as eye movements suggests that the working memory hypothesis is a likely mechanism of action as they both involve taxing the working memory system. However, it is important to note that studies have not yet implemented alternative tasks in the full EMDR procedure and as such it is unclear whether such tasks could replace eye movements in the full treatment. These studies need to be conducted involving patients with PTSD in order to draw such conclusions.

Optimizing Implications

Optimizing Treatment

It may be that optimal results are regulated by modality-specific interference in EMDR, in which the modality of the task is aligned with the modality of the trauma. For example, auditory taxation has been found to be less effective than visual taxation at decreasing emotionality and vividness of visual images, but more effective than visual taxation for auditory images (Homer et al., 2016; Kemps & Tiggemann, 2007). Although this concept has been criticised, with some studies showing no benefits to aligning modalities (Gunter & Bodner, 2008), no firm conclusions can be drawn until stronger studies are conducted, and their findings are replicated. Until then, it may be useful to primarily use eye movements or visuospatial tasks, given that visual intrusions are the most common, positively affecting between 70 and 97% of patients (Ehlers et al., 2002). Although, given that memories do occur in different modalities, it is important for further research to investigate the effects on memories of a visual, auditory, and even tactile nature in order to optimise treatment.

Another potential way of optimising outcomes may be to alter the working memory load, as a certain degree of working memory taxation may be necessary for optimal results. Performing fast eye movements has been shown to reduce the vividness and emotionality of an autobiographical memory to a greater degree than slow

eye movements (Maxfield et al., 2008; Patel & McDowall, 2016; van Veen et al., 2015). This suggests that faster eye movements that were more difficult resulted in greater exhaustion of the visuospatial sketchpad. However, van den Hout et al. (2010) demonstrated that simple counting led to slightly greater reductions in emotionality than complex counting, suggesting that there is an optimal level of taxation, beyond which reductions in emotionality are less prevalent (Gunter & Bodner, 2008). Conversely, Littel and Van Schie (2019) demonstrated a linear relationship between working memory taxation and reductions in the vividness and unpleasantness of memories.

Therefore, further research is warranted to determine whether more taxing tasks induce better results, whether outcomes are affected by working memory capacity, and whether there is an optimal degree of taxation.

Increasing Access to EMDR by Using Alternative Methods to Eye Movements

The fact that eye movements do not seem to be strictly necessary for EMDR has implications for increasing access to EMDR. Firstly, it may be more accessible for individuals who have difficulty with eye movements, such as those with a disability. Secondly, there are limitations in accessing EMDR by qualified therapists and it may be that replacing eye movements makes EMDR easier to self-administer. The limited accessibility is partly due to the limitations associated with training EMDR therapists, as identified in qualitative research of EMDR training in the United Kingdom and Ireland (Farrell & Keenan, 2013). For example, several NHS nurses believed there was no added value in EMDR training with regard to their career development. This limits the number of qualified specialists in EMDR that are unable to help the high number of individuals requiring treatment. As a result, patients have attempted to self-administer EMDR, evidenced by numerous online forums such as 'my PTSD'. They may use audio files to produce bilateral auditory stimulation and butterfly hugs to produce tactile stimulation, the latter of which has been supported for various dysfunctional memories of man-made and natural disasters (Jarero & Artigas, 2012). The use of the butterfly hug could be taught in schools to benefit pupils who have experienced distressing events. Thus, identifying whether tactile stimulation is beneficial could be important for increasing access.

Although the use of self-administered approaches is promising, it is important to consider the associated risks, with Shapiro (2001) suggesting that adequate screening, preparation (where the therapist builds a therapeutic relationship with the patient and prepares them for EMDR), and implementation is necessary to prevent fatal consequences. However, without a solid evidence base for the risks of EMDR delivered without rigour, it is unclear whether it does have such harmful effects. Shapiro (2012)

developed self-help books which promote the unsupervised administration of the preparation phase of EMDR. This may offer a way to save specialists time and make EMDR more widely accessible in order to improve access for all individuals with PTSD. Furthermore, if eye movements are not necessary in the RDI phase, this phase could be achieved without direct contact with a therapist and could even be implemented as part of a stepped care approach. This would require dismantling studies to determine whether certain aspects of the EMDR process are effective alone for certain individuals, and whether this is the case for all types of stimulation rather than just eye movements. These implications lend further credence to the necessity of further research into this topic, and the importance of this review.

Conclusion and Future Directions

This review investigated the use of eye movements in EMDR, with evidence suggesting that they are valuable for increasing the efficacy of EMDR. However, while this suggests that they are important, it does not mean that they are necessary. This is important as eye movements are generally clinically disliked, and thus identifying alternative methods may help to improve clinical acceptability and tolerability, especially amongst individuals with PTSD. The EMDR procedure states that other forms of stimulation can be used to replace eye movements, including auditory and tactile stimulation. Both auditory and tactile stimulation have been found to reduce vividness and emotionality of memories, highlighting the potential alternative forms of stimulation have in actuating positive effects. However, the evidence supporting alternative forms of stimulation is limited due to the low number of studies conducted and the limitations of these studies.

Stronger evidence has been obtained for the use of alternative dual attention tasks, which do not necessarily involve alternating bilateral stimulation, due to the greater number of studies conducted. Therefore, it may be possible to replace eye movements in EMDR with these tasks, such as counting. However, this has not been tested in treatment studies with the full EMDR procedure and are not currently recommended in the EMDR protocol. Furthermore, there is indication that eye movements are superior to non-visuospatial tasks, which may be linked to the notion of modality specificity. Therefore, it may be preferable to use visuospatial tasks, but this needs a greater evidence base to draw stronger conclusions. It would be useful to establish whether alternative dual tasks could be used as an equally effective alternative to eye movements or if they would be an inferior choice.

The controversy surrounding the necessity of eye movements stems from methodological weaknesses, great heterogeneity, and clear gaps in the current research. Four key areas are proposed as the most prominent future

directions to advance this field.

1. Laboratory studies need strong methodological rigour

Laboratory studies are important as they can use large sample sizes of healthy participants with appropriate control groups. Firstly, *priori* power analyses should be conducted to ensure that all studies have sufficient statistical power. Secondly, it would be valuable for future laboratory studies to focus only on negative autobiographical memories and positive cognitions, to better resemble the effects of eye movements, auditory and tactile stimulation in EMDR (stage 4 and 5 respectively), and to use both subjective and objective measures to prevent biases from subjective measures while also maintaining the predictive validity of subjective measures (given that subjective units of distress are used in EMDR). Thirdly, it would be beneficial to use two control groups, one involving recall only, and one not involving recall at all. This would ensure that the effect cannot be attributed to recall alone or to time.

2. Laboratory studies should be qualified by highly controlled treatment studies

Laboratory studies should then be qualified with treatment studies, where fully trained therapists administer the full EMDR procedure to patients with PTSD, measuring the same outcome measures as well as both immediate and long-term remission rates. This refers to the number of patients who no longer meet diagnostic criteria immediately following treatment, and in the long-term to ensure that the effects of EMDR persist. These outcomes should be compared to those of patients receiving the same treatment without eye movements, as well as those on a wait-list for treatment, to ensure that the effects cannot be attributed to time. This would help to conclusively support the premise for the addition of eye movements in EMDR.

3. More studies assessing auditory and tactile stimulation are needed

Once this has been established, efforts should be made to determine whether auditory or tactile stimulation are effective in EMDR. This research is currently lacking. Studies should adopt the same approach as for eye movements, replacing eye movements with auditory or tactile stimulation. If they are shown to be effective, they should then be directly compared with eye movements to determine whether they are equally as efficacious.

4. Treatment studies should implement alternative dual tasks

Laboratory studies have demonstrated the efficacy of alternative dual tasks, but treatment studies are needed involving patients with PTSD. If they are efficacious for

use in EMDR, questions regarding optimising treatment through the difficulty of the task and the modality of the task should be investigated.

Abundant research is needed to drive this field of research forward and optimise EMDR treatment. Conducting studies using consistent methodologies will enable stronger conclusions to be made about the necessity of eye movements in EMDR. Although much more research is needed, these should be the first steps taken to offer stronger evidence towards the utility of alternative stimulation or alternative tasks in EMDR, especially amongst individuals with PTSD.

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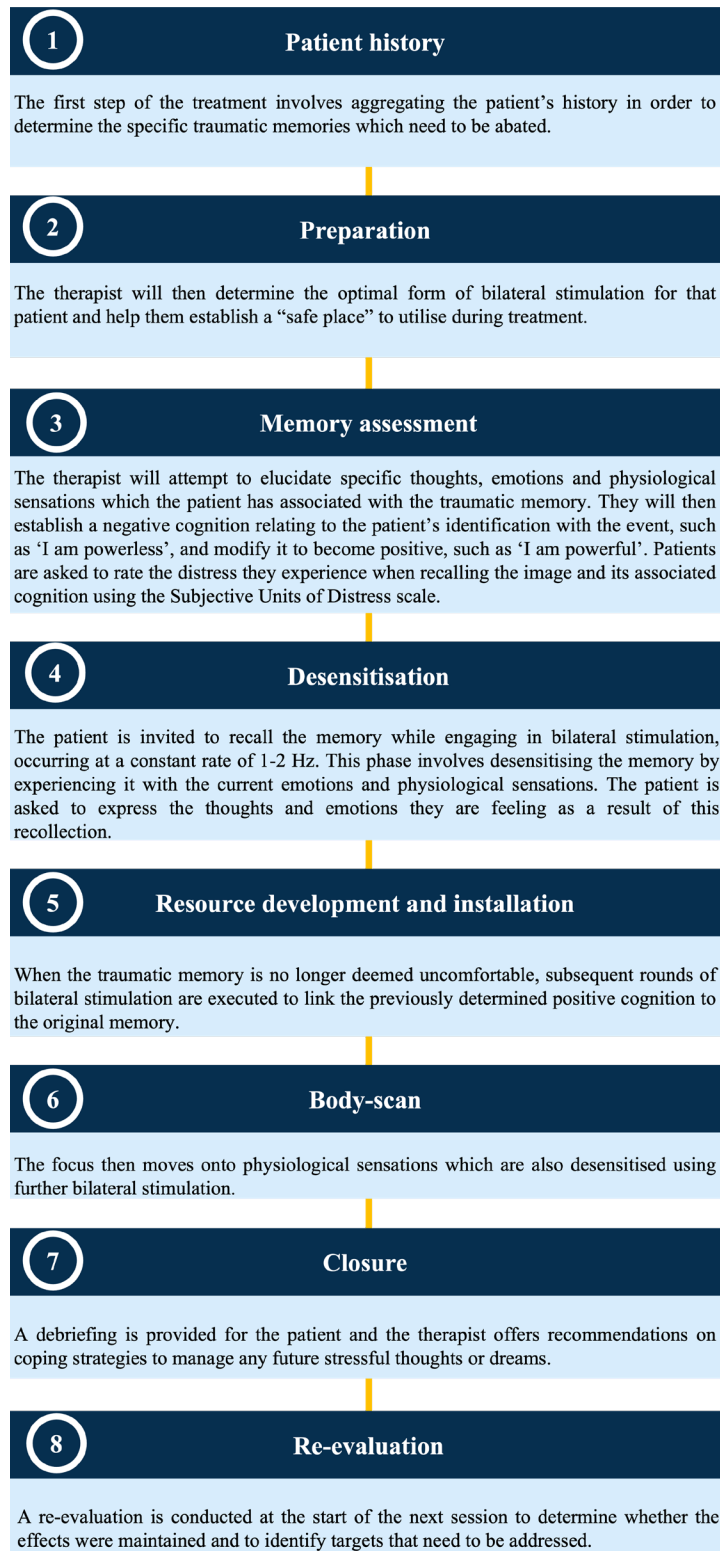
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Appendix

Figure 1

The full EMDR treatment procedure. Source: Author produced, adapted from Shapiro (2017).



Amber Korde, BA University of Oxford

Graduated with first class honours in June 2021.

Amber Korde graduated with first class honours from the University of Oxford in June 2021 with a Bachelor of Arts in Experimental Psychology. She is attending University College London (UCL) in September of 2022 to study a Doctorate in Clinical Psychology. Amber currently works for the charity Mind as a Mental Health Crisis Worker, supporting anyone in Oxfordshire who is experiencing a mental health crisis. In her free time Amber likes to spend time with her friends and is looking forward to an exciting move to London in September!



Was there a particular experience that sparked your research interests?

I was initially inspired to research postpartum psychosis after watching the BBC Documentary 'My Baby, Psychosis and Me'. After watching this, I began researching more and more into the experiences of women who develop psychosis symptoms after childbirth. The thing that struck me the most was the level of stigma these women face, and the lack of education the general public has about the disorder. I hope that the dissemination of my research can add something to the field, and shed some more light on a very important topic.

Who has been the most influential person in your life?

So many people in my life have been influential in shaping who I am today. My parents and Ellis for their continued support at every hurdle, and shaping me into who I am. My best friend Georgia, for convincing me every step

of the way that I am more capable than I think and to believe in myself. Amy, Bekah, Emilia, alongside Georgia, for friendship that will last a lifetime. Catrin and everyone in Oxford for being there for every up and down throughout our time at Oxford!

What is your greatest accomplishment?

I hope that my greatest accomplishments are ahead of me but to date my proudest moment has been being accepted onto the Doctorate in Clinical Psychology just one year after finishing my undergraduate degree. I am so grateful to have been given this opportunity and cannot wait to see where it takes me!

Where do you see yourself in 10 years?

I can honestly say I have no idea! In 10 years time I will be a qualified clinical psychologist after completing my doctorate in clinical psychology. I will hopefully be working within the NHS in a job I am passionate about, supporting service users with their mental health.

Risk Factors for Postpartum Psychosis: A Systematic Review

Amber M. Korde

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Postpartum psychosis (PP) is a serious mental illness occurring in the postpartum period that can result in serious adverse outcomes for both the mother and baby¹. It is important to understand the factors which increase the risk of developing PP in order to target primary prevention strategies and minimize the likelihood of adverse outcomes for mother and baby. This systematic review seeks to establish, through the available literature, what the risk factors are for the development of postpartum psychosis in adults over the age of 16. Primary studies up to January 10th 2021 to be included in the review were identified through MEDLINE, EMBASE and PsycInfo. Studies included in this review recruited pregnant women over the age of 16 and had at least one potential risk factor as an exposure variable and psychosis during the postpartum period as the outcome measure. Of the 951 studies identified, 35 studies with a total of 88 observations were included in the review. A total of 14 potential risk factors had sufficient observations to be explored with 11 factors yielding inconsistent results and 4 factors showing consistent results across observations. Personal history of psychotic illness and severity of previous bouts of psychiatric illness were consistently identified as significant risk factors for postpartum psychosis. Marital status and type of delivery were consistently found to have no relationship with PP. These findings offer novel insight into risk factors for PP. Other potential risk factors yielded mixed results and are thus considered inconclusive at this time. The novel finding that severity and recency of previous illness is consistently identified as a risk factor should inform future interventions.

Keywords: Post-Partum Psychosis, Risk factors, Puerperal Psychosis, Systematic Review

The postpartum period for women involves substantial physical, biological, emotional, and social changes and has been identified as a period of vulnerability for a range of psychiatric disorders such as "maternity blues," postpartum depression, and postpartum psychosis (Rodriguez-Cabezas & Clark, 2018). Psychosis can be defined as "an abnormal condition of the mind that results in difficulties determining what is real and what is not" (Arciniegas, 2015). Psychosis can occur within several disorders as well as postpartum psychosis, including schizophrenia, bipolar disorder, or schizoaffective disorder. Postpartum psychosis (PP) is characterised by a dramatic and rapid onset, increasing deterioration of mental health, and symptoms such as hallucinations, delusions, depression, and

disorganized behaviour (di Florio et al., 2013). The classic picture of a mother with PP was described by Brockington (1996) as "an odd affect, withdrawn, distracted by auditory hallucinations, incompetent, confused, catatonic; or alternatively, elated, labile, rambling in speech, agitated or excessively active." The mother may have strongly-held beliefs centering around themes of childbirth such as a sense of persecution from the baby or a sense of their baby's altered identity. Indeed, Wisner et al. (1994) found that women with postpartum onset of psychosis experienced unusual psychotic symptoms and cognitive disorganization. The typical onset of PP is between three and ten days post-birth (Veerle Bergink et al., 2011), although studies investigating PP often employ a wider

¹This author is aware of the existence of pregnant people who do not identify as women. Consulted literature in this review focuses solely on pregnant women and thus for the purpose of this study, I will refer to pregnant women exclusively.

time frame (e.g., Nager et al., 2005; Meltzer-Brody et al., 2017). The prevalence of PP is estimated to be between 0.89 and 2.6 women per 1000 births (VanderKruik et al., 2017). Despite its rarity, PP is regarded as one of the most severe mental health problems that occurs postpartum with episodes of PP that are unmanaged or poorly managed increasing the risk of infant and maternal accidents as well as maternal suicides (Brockington, 2017). The Confidential Enquiry into Maternal Deaths (CEMD) estimates that two in every 1000 women who experience PP die by suicide (CEMD, 2001). Additionally, the risk of infanticide, although remaining very rare, is elevated in the presence of PP (Sit et al., 2006). A clinical survey of mothers experiencing PP found that, among women hospitalized for PP, 28% to 35% described delusions relating to their infant but only 9% had thoughts of harming their child (Kumar et al., 1995). PP may also result in maternal neglect of their infant's needs or unsafe behaviors and adversely affect mother and baby bonding (Carter et al., 2001). PP is typically characterized much like psychosis in that women experience delusions and hallucinations. However, the presentation varies significantly among women, as PP can present more like bipolar disorder. Indeed, Sit and colleagues (2006) argue that PP is an overt presentation of bipolar disorder that occurs at the time of large hormonal shifts which occur post-delivery. Other literature has indicated that considerable biological investigation may be necessary in women presenting with psychotic symptoms postpartum in order to exclude organic causes of their symptoms such as infection (Subramanyam et al., 2020), autoimmune encephalitis (Bergink et al., 2011), and thyroiditis (Bokhari et al., 1998).

In light of the severity of PP and the potentially disastrous consequences if left untreated, it is essential that proper identification and management of PP takes place. Thus, early identification of women with PP or women at an increased vulnerability of developing PP is crucial in order to minimize these risks. Women with PP are considered to be in a "psychiatric emergency" (Heron et al., 2008) and require immediate assessment and typically psychiatric admission in order to manage symptoms. The identification of risk factors are important to predict, prevent, and allow early intervention for mental illness (Offord and Kraemer, 2000).

Reliable identification of the risk factors associated with PP and women who may be at an increased vulnerability is paramount to the success of clinical or public health interventions. Various risk factors have been considered such as history of psychosis, pregnancy and obstetric complications, primiparity, type of delivery, stressful life events, and many more (Vikstrom et al., 2017; Nager et al., 2008; Kendell et al., 1987; Kendell et al., 1981; Aas et al., 2020; Işık, 2018). However, the risk factors related to PP remain poorly understood with a large number of conflicting reports and a lack of consistent findings across studies. The National Institute for Health and Care Excellence (NICE) recommendations have identified a better understanding of the risks of PP for primary prevention as a research priority, so this question is at the forefront

of the research agenda (NICE, 2016). The National Health Service webpage on PP states an increased risk for women who: have familial history of mental illness or PP, have a personal history of bipolar disorder or schizophrenia, have experienced a traumatic birth or pregnancy, or have developed PP following a previous pregnancy (*Postpartum Psychosis – NHS n.d.*). Despite these factors being generally considered to increase the risk of PP, there are no current systematic or non-systematic reviews which investigate whether they are consistently and significantly associated with increased risk. The identification of stable risk factors that are present pre-delivery can enable clinicians to provide care before the postpartum period. Informing women and their families of symptoms of PP to be aware of and potential treatment options may allow earlier identification and treatment (Yonkers et al., 2004). If labor or post-birth related factors are identified as increasing the risk for PP development, post-delivery interventions can be developed in the immediate postpartum period in order to prevent PP from developing or to manage symptoms. Identifying further risk factors will enable more accurate care to be delivered both pre-delivery and immediately following delivery.

One method used to identify consistent risk factors for a given condition is a systematic review. A systematic literature review seeks to "identify, appraise and synthesise all the empirical evidence that meets pre-specified eligibility criteria" (*About Cochrane Reviews* - Cochrane Library, n.d.). Conducting a robust systematic review allows us to identify the current literature, its limitations, quality, and future directions and can be an important tool in the development of clinical interventions. To our knowledge, no previous studies have conducted a systematic review synthesizing all available literature relating to risk factors for PP. This review will assess the current literature on risk factors for PP in order to identify any variables that increase women's vulnerability to developing PP. The results of this review have important implications for future clinical practice.

Method

Review Question

The objective of this review was to describe and evaluate the risk factors of postpartum psychosis using findings from published studies. The review question for this work was: what are the relevant risk factors for the development of postpartum psychosis in adults over the age of 16?

Search

Prior to the initiation of this study, a pilot scoping review was conducted in November 2020 to discern whether there was sufficient available index literature to make a systematic review feasible. An initial search strategy was established in accordance with the PEO Population, Exposure, Outcome) framework. (Bettany-Saltikov & McSherry, 2016). The PEO framework

is useful to identify searchable parts of a research question, refine results, and focus the review process. Review search terms were defined through an iterative process. A literature review and consultation with clinical experts created an initial set of terms, and these terms were further refined by scanning studies that were identified in the scoping search and modifying the terms until all studies identified in the pilot search were captured and a balance between sensitivity and specificity of the search was reached. The final search was conducted via Ovid, searching the databases MEDLINE, EMBASE, and PsycInfo, without language or date restrictions from inception to 10th January 2021. This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Page et al., 2021).

Selection criteria

Studies included were required to have postpartum women over the age of 16 as their study population and to investigate the association between any given variable and postpartum psychosis. Women over the age of 16 were chosen as the study population as research has shown that women who give birth when they are minors experience worse mental health outcomes compared to women over 16 (Boden et al. 2008). Therefore, the decision was made to exclude participants under 16 to avoid possible confounders that may influence poor maternal mental health in underage delivery such as high risk pregnancy and birth (Mohammadi et al. 2016), inadequate social support (Sekhoetsane, 2012), and social stigma (Vincent & Alemu, 2016). Studies were eligible if they were primary research studies of any study design that identified at least one potential risk factor as their exposure variable and used postpartum psychosis as their outcome measure. Excluded studies were any not focusing on postpartum psychosis, not focusing on the postpartum period, studies of very low methodological quality (based on the quality assessments described below) and studies that did not include primary data (e.g., reviews).

Screening

Search results were first imported into Mendeley Desktop (v1.19.8) in order to remove duplicates and then imported into Rayyan (Ouzzani et al., 2016) for screening. Titles and abstracts were screened alongside a second independent reviewer. Discrepancy between reviewers was resolved by discussion. Full-text screening of selected studies was carried out by the primary researcher with any uncertainties resolved by the second reviewer.

Data Extraction

Key information extracted were study population, study design, year, setting, participant characteristics, sample size, method of assessing postpartum psychosis, details of exposure

to risk factor, and outcome variable (postpartum psychosis). The outcome of interest in this review was the presence of psychosis with the onset in the postpartum period.

Assessment of study quality

The methodological quality of each study was assessed by a single reviewer on the basis of a checklist that follows the Critical Appraisal Skills Programme of the British National Health Service (CASP UK, n.d.). This checklist uses 7 criteria to assess four domains: measurement bias, confounders, attrition bias (for cohort studies), and recruitment bias. The criteria used can be seen under Assessment Criteria in Figure 2. Studies that met 5 or more criteria were rated as high quality, studies meeting 3 or 4 were rated as moderate and studies meeting less than 3 were rated as low. For case-control and cross-sectional studies, only 5 criteria applied (excluding assessments of attrition bias); studies that met 4 or more were rated as high, studies meeting 2 or 3 rated as moderate, and studies meeting less than 2 rated as low. Assessments of quality are presented in figure 2.

Data synthesis

In accordance with recommendations from the Cochrane Collaboration, for every potential risk factor, the evidence was categorized as insufficient if fewer than three observations on a single characteristic were considered in the review (Hölzel et al., 2011). If three or more observations were considered and the ratio of positive to negative findings was at least four to one, the characteristic was categorized as consistent. For variables which yielded a more balanced ratio of positive to negative findings, the characteristic was categorized as inconsistent. Characteristics which indicated an association with PP in a consistent direction were considered as a risk factor. Positive findings were considered to be statistically significant findings of an association between the given risk factor and PP. Negative findings were considered to be the absence of any statistically significant association between the given risk factor and PP.

Results

Study selection

In the initial search through the databases MEDLINE, EMBASE, and PsycInfo, 965 studies were identified. A total of 14 duplicates were then removed, leaving 951 articles to be screened by title and abstract. After initial screening by title and abstract, 64 studies remained. These remaining articles were screened by full-text, leaving 35 studies to be included in the final review (appendix 1). Reasons for exclusion at the full-text screening stage were: 3 studies did not include primary data, 6 studies employed non-experimental study designs (typically qualitative studies), 7 did not assess risk factors for postpartum psychosis, 6 employed the wrong outcome

measure (i.e. did not measure outcome of PP), 4 had unavailable full-text articles, and 3 had insufficient data. The majority of these studies investigated more than one potential risk factor, yielding a total of 88 observations included in the final review. A total of 30 potential risk factors were identified with 15 having sufficient observations in order to be assessed. These 15 potential risk factors are discussed below. A table describing all studies included in this review can be found in the appendix (appendix 1). The total number of participants across all 56 studies was 7,228,210 primarily due to the large number of nationwide register-based study designs such as Valdimarsdóttir et al. (2009) and Meltzer-Brody et al. (2017). The sample sizes ranged from 30 (Aas et al., 2020) to 5,246,97 (Warselius et al., 2019).

Figure 1

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of study selection process

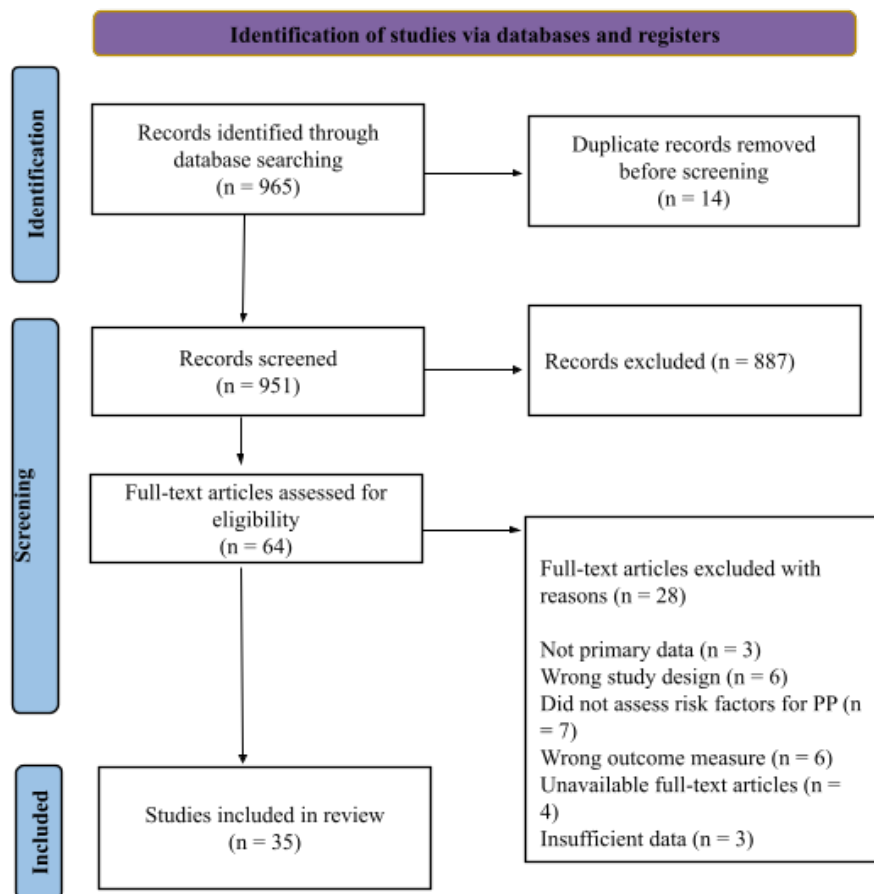


Figure 2

Assessment of quality following the Critical Appraisal Skills Program

Study:	Measurement bias		Confounders	Attrition bias		Recruitment		Global assessment
	Y	N		Y	N	Y	N	
McNeil (1986) - 1	Y	Y	N	ND	ND	Y	Y	Moderate
McNeil (1987) - 2	Y	Y	Y	ND	ND	Y	Y	High
McNeil (1988) - 4	Y	Y	Y	ND	ND	Y	Y	High
McNeil (1988) - 5	Y	Y	Y	ND	ND	Y	Y	High
McNeil (1988) - 3	Y	Y	Y	ND	ND	Y	Y	High
McNeil (1988) - 6	Y	Y	Y	ND	ND	Y	Y	High
Morris (2020)	Y	Y	Y	ND	ND	Y	Y	High
Meltzer-Brody (2018)	Y	N	Y	N/A	N/A	Y	Y	High
	Y	Y	Y	ND	ND	Y	N	Moderate
Allwood (2000)	Y	Y	Y	N/A	N/A	Y	Y	High
Nager (2005)	Y	Y	Y	N/A	N/A	Y	Y	High
Hellerstedt (2013)	Y	N	Y	N/A	N/A	Y	Y	High
Lewkowitz (2019)	Y	N	Y	N/A	N/A	Y	Y	High
Lewkowitz (2019)	Y	Y	Y	N/A	N/A	N	Y	High
Di Florio (2018)	Y	Y	Y	N/A	N/A	Y	N	Moderate
Aas (2020)	Y	N	Y	N/A	N/A	Y	Y	High
Brown (2019)	Y	Y	N	Y	ND	Y	N	Moderate
Mighton (2015)	N	Y	Y	N/A	N/A	Y	Y	High
Sharma (2004)	Y	Y	Y	ND	ND	Y	Y	High
Marks (1992)	Y	Y	Y	ND	ND	Y	Y	High
Agrawal (1990)	Y	Y	Y	N/A	N/A	Y	Y	High
Upadhyaya (2014)	Y	Y	Y	N/A	N/A	Y	Y	High
Kendell (1981)	Y	Y	Y	N/A	N/A	Y	Y	High
Kendell (1987)	Y	Y	Y	N/A	N/A	Y	Y	High
Kirpinar (1999)	Y	Y	Y	N/A	N/A	Y	Y	High
Valdimarsdottir (2009)	Y	N	Y	N/A	N/A	Y	Y	High
Vilkstrom (2017)	Y	Y	Y	N/A	N/A	Y	Y	High
Harlow (2007)	Y	Y	N	N/A	N/A	Y	Y	Moderate
Dowlatashi (1990)	Y	Y	Y	ND	ND	Y	Y	High
Marks (1991)	Y	Y	Y	N/A	N/A	Y	Y	High
Warselius (2019)	Y	Y	Y	N/A	N/A	Y	Y	High
Nager (2006)	Y	Y	N	ND	ND	Y	N	Moderate
Kumar (1993)	Y	Y	Y	N/A	N/A	Y	Y	High
Nager (2008)	Y	Y	Y	N/A	N/A	N	N	Moderate
Blackmore (2006)								

Assessment Criteria:**Measurement bias:**

- Did a valid and reliable measurement of the exposure to the risk factor take place?
- Did a valid and reliable measurement of the outcome take place?

Confounders:

- Did the authors identify all important confounding factors and take account of them in design and/or analysis?

Attrition Bias (longitudinal cohort studies only):

- Were drop-out rates in both groups similar?
- Are there no systematic differences between completers and those who dropped out?

Recruitment:

- Were the participants recruited into the study consecutively or randomly selected?
- With respect to the following features, do the study participants represent a representative sample of the total population?

Key:

Y = yes

N = no

ND = no data given

N/A = not applicable

Consistent findings:

Personal history of psychotic illness

A total of 7 studies assessed the risk of personal history of psychotic illness for postpartum psychosis, with consistent findings. All 7 of these studies found evidence that personal history of psychosis or other disorders with symptoms of psychosis is a risk factor for postpartum psychosis. A longitudinal cohort study of 192 women by McNeil (1986) found that the difference in rates of PP in women with a previous history of non-organic psychosis and matched controls was highly statistically significant ($P < 0.0005$). Vikström et al. (2017) conducted a nationwide register-based cohort study and found that, among primiparous women who underwent IVF treatment in Sweden, the risk of PP was significantly increased among women with a history of psychotic disorder ($P < 0.001$; $OR = 324.1$; 95% $CI = 131.3-800.0$) and women with a history of bipolar disorder ($P < 0.001$; $OR = 516.1$; 95% $CI = 264.3-1008.1$). Allwood et al. (2000) investigated the effect of personal psychotic history as a risk factor for PP in Black African women in Johannesburg, South Africa and found a significantly higher incidence of prior psychotic illness in patients with PP than in women who remained well in the postpartum period ($P < 0.0001$). Allwood's findings suggest that the finding of previous psychotic illness as a risk factor in many Western studies may be generalizable outside of this context. di Florio et al. (2018) employed a retrospective cohort design and found that women with a history of affective psychosis in the perinatal period are six times more likely to develop a recurrence of PP in subsequent pregnancies than women without any prior history of psychotic episodes in the perinatal period. Three other studies only used descriptive statistics when reporting findings which indicated personal history of psychotic illness as a risk factor for PP. Marks et al. (1991), for example, found that, among pregnant women from London hospitals, all cases of PP occurred in women with prior history of bipolar disorder or schizoaffective disorder, making up 46% of the total sample of women with a history of bipolar or schizoaffective disorder. This indicates that women with psychiatric history of psychosis may be at a higher risk of PP. A subsequent study from Marks et al. (1992) found that, among a sample of 88 women, all cases of PP had experienced past episodes of mania, hypomania, or schizomania as well as having a previous diagnosis of bipolar disorder or schizoaffective disorder. Research from Sharma et al. (2004) further evidenced an increased risk among these groups, finding that 60% of all women admitted to hospital with a diagnosis of PP had suffered previously from bipolar disorder or schizoaffective disorder. All articles included in this study which investigated women with a personal history of psychosis or related disorders reported an increased risk for PP among these women. Six of these seven studies were assessed as having high methodological quality. Based on the studies identified here, there is consistent evidence that suggests the role of personal history of psychosis, or related disorders, as a risk factor for PP.

Characteristics of previous psychiatric illness

Characteristics of previous periods of psychiatric illness were explored in 5 studies with a significant association between severity or recency of prior illness and PP reported in all observations. The specific variables investigated in these studies were: illness recency, hospitalization length, severity of illness, and number of psychiatric episodes per year. Hellerstedt et al. (2013) reported that, for primiparous women in Sweden with prior psychiatric hospitalization, more recent, longer term, and multiple pre-conception psychiatric hospitalisations were independently associated with PP hospitalisations ($OR = 3.22$, $CI = 2.07-5.01$, $OR = 1.90$, $CI = 1.22-2.95$, $OR = 5.09$, $CI = 3.38-7.67$, respectively). McNeil (1987) reported that the development of current PP was related to more than 3 months hospitalisation ($P < 0.005$), the existence of mental disturbance during the 6 months prior to conception ($P < 0.0005$), and previous psychiatric illness reaching the most severe degree of disturbance ($P < 0.05$). di Florio et al. (2018) carried out a retrospective cohort design and also found statistically significant associations between PP and the number of episodes per year of psychiatric illness pre-conception ($\beta = 0.4070$; $s.e. = 0.141$; $z\text{-value} = 2.893$; $P = 0.004$). Harlow et al. (2007) found that, in Swedish first-time mothers, the risk of developing PP increased with more recent psychotic hospitalisations ($p < 0.001$), greater frequency of hospitalisations ($P < 0.001$), and longer length of the most recent psychiatric stay ($P = 0.01$). Marks et al. (1992) reported that women who developed psychosis in the postpartum period had more recently been admitted to psychiatric units compared to women with prior psychiatric history who remained well postpartum ($t = 2.10$, $df = 28$, $P < 0.05$). All 5 of the studies exploring characteristics of previous psychiatric illness report significant findings. Thus, we can categorise severity and recency of prior psychiatric illness as risk factors for PP. However, it is important to recognize that this conclusion would benefit from meta-analyses or from a wider pool of research in order to strengthen this assertion.

Marital status

The relationship between marital status at time of delivery and PP was investigated in 3 studies with a lack of association reported in all 3. Two studies by Kendell and colleagues (1981; 1987) investigated whether marital status was a risk factor for the development of PP with findings displaying a lack of significant association in both cases. Additionally, McNeil, (1987) reported no significant differences were found between women who developed PP and controls who remained well in marital status ($P = 0.137$). These findings are consistent and thus we suggest that marital status is not a risk factor for the development of PP. However, this conclusion would benefit from further inference through meta-analysis or from a wider pool of research.

Type of delivery

Several studies examined type of delivery as a potential risk factor for PP with 5 studies reporting a lack of significance and 2 reporting a significant association between the two. A population-based cohort study by Kendell et al. (1981) reported that caesarean section was significantly associated with psychosis in the postpartum period ($P < 0.01$). Nager et al. (2008) identified the same relationship, reporting a significant difference in rates of PP among women who had caesarean sections and those who did not ($P < 0.001$). However, the remaining 5 studies failed to find any significant results with regard to type of delivery. Upadhyaya et al. (2014) and Vikstrom et al. (2017) both reported that type of delivery (caesarean vs natural) was not associated with PP. Blackmore et al. (2006), Valdimarsdóttir et al. (2009), and Kendell et al. (1987) all reported that exposure to caesarean section was not statistically significant in increasing the risk of PP development. Overall, the studies show a lack of significance at the ratio 5:2 and thus we can consider type of delivery as consistent (as specified in the methods) and tentatively conclude that type of delivery is not a risk factor for PP, although this conclusion would benefit from further inference through meta-analysis or from a wider pool of research.

Mixed results:

Personal history of non-psychotic mental illness

A total of three studies provided observations on personal history of non-psychotic psychiatric illness as a potential risk factor for PP with mixed findings. Vikstrom et al. (2017) provided the most rigorous assessment of history of non-psychotic psychiatric illness as a risk factor for PP, running multiple logistic regression analyses for all psychiatric disorders grouped together and for the individual disorders separately. They found that, among primiparous women who underwent IVF treatment in Sweden, the risk of PP significantly increased in women with a history of any psychiatric disorder (OR; 40.726, CI; 23.866–69.496, $P < 0.001$). The risk was also significantly increased in women with schizophrenia or other psychotic disorder ($P < 0.001$; OR=324.1; 95% CI=131.3–800.0), bipolar disorder ($P < 0.001$; OR=516.1; 95% CI=264.3–1008.1), depression ($P < 0.001$; OR=27.5; 95% CI=16.2–46.5), anxiety ($P < 0.001$; OR=12.9; 95% CI=7.4–22.6), or personality disorder ($P < 0.001$; OR=27.3; CI=11.8–63.0). Mighton et al. (2016) carried out a prospective longitudinal cohort study and reported positive findings for history of non-psychotic psychiatric illness as a risk factor, finding that, among primiparous women with a history of major depressive disorder (MDD), 23% of their sample scored above threshold for psychosis during the postpartum period. This, they argued, suggests an increased risk for developing PP among women with a history of MDD as the prevalence of PP in the general population is estimated at 0.1–0.2%. However, results from Marks et al. (1992) report

conflicting findings. Marks and colleagues found that among 47 women with a history of affective disorder and 45 controls, 12 developed PP. None of the 12 cases had a history of any non-psychotic psychiatric disorder, leading them to conclude that this does not represent an increased risk of PP. However, these null findings may represent an insufficient sample size for the investigation of the risk of non-psychotic psychiatric illness as only 12 women in their sample developed PP. With few studies reporting on risk of non-psychotic illness and its association to PP, we were unable to conclude non-psychotic illness as a risk factor for PP based on lack of evidence.

Family history of psychiatric illness

In this review, three studies were included which investigated a familial history of psychiatric illness as a potential risk factor for PP with mixed findings. Upadhyaya et al. (2014) carried out a cross-sectional case control study among women in India presenting with psychiatric disturbances and found that a positive family history of psychiatric illness was not associated with increased risk of PP ($P = 0.44$). The non-significant association was also seen in a retrospective cohort study by Kirpinar et al. (1999) among women in Turkey with first-case postpartum psychosis. Kirpinar et al. reported no significant differences between women with PP and controls with regard to positive familial history of psychiatric disorders. The third article identified to explore mental illness in relatives did, however, report significant findings. Allwood et al. (2000) carried out a two-part study with a retrospective and prospective design. They reported significantly higher incidences of family psychiatric history in women who had developed PP compared to controls ($P < 0.05$). In summary, the mixed observations regarding family history of psychiatric illness prevent us from concluding whether mental illness in family can be considered a risk factor or not.

Parity

Parity, or number of live born children, was investigated by 7 studies with mixed findings; 4 studies identified a significant association between primiparity (birth of first child) and developing PP, and 3 studies failed to show this association. Kendell et al. (1981) carried out a population-based cohort study of 704 women residing in Edinburgh and reported that primiparity was significantly associated with patients with PP ($P < 0.01$). A later study by Kendell in 1987 replicated these findings, observing a heightened risk in primiparity with all psychiatric admissions and each of the psychoses sub-groups showing a significant excess of first-time mothers ($P < 0.05$). Similarly, Upadhyaya et al. (2014) found that parity status was significantly associated with PP, with primiparous women more likely to develop PP ($P = 0.02$). Blackmore et al. (2006) found the same associations among high-risk women. They carried out a retrospective study of 129 women with lifetime diagnosis of bipolar or schizoaffective disorder and reported a significant

association with primiparity and developing PP (OR 3.76, CI; 1.94-7.27, $P < 0.001$). However, 3 other included studies failed to observe significant findings regarding parity and PP. Marks et al. (1992) reported that parity was not associated with an increased risk of psychiatric relapse among women with histories of affective disorders. Additionally, McNeil, (1987) and Allwood et al. (2000) both independently reported a lack of significant difference with regard to parity between women with PP and controls. In summary, there are mixed findings regarding parity as a risk factor for PP, and thus it remains inconclusive as to whether parity is a reliable risk factor or not.

Maternal age at delivery

Maternal age at delivery was investigated in 8 studies, yielding mixed results with 4 studies reporting a significant association between maternal age and PP and 4 studies failing to find an association. Sharma et al. (2004) reported that there was no significant difference in the mean age of women admitted to hospital with a diagnosis of puerperal psychosis and women who remained well in the postpartum period. Hellerstedt et al. (2013) carried out a large nationwide register-based cohort study of 1842 women and found no significant difference in mean age between groups (mean 29.7, SD 4.8, and mean 29.6, SD 5.4, $P = 0.79$). Observations from McNeil, (1987) and Kirpinar et al. (1999) further revealed a lack of significant difference in maternal age among women with PP and women without. However, three studies identified a significantly increased risk of PP among women with higher maternal age. Two large nationwide register-based cohort studies by Nager et al. (2006, 2005) revealed a higher risk of hospitalisation with higher maternal age (HR = 6.56 (CI=3.1-13.8, HR; 7.36 (95% CI; 3.73–14.53 $P < 0.0001$)). Valdimarsdóttir et al. (2009) also found that higher maternal age significantly increases the risk of PP (HR = 2.4, 95% CI 1.2-4.7). Interestingly, Upadhyaya et al. (2014) found a significant effect of maternal age on risk of PP but in the opposite direction, reporting that lower maternal age was significantly associated with PP ($P = 0.001$). In light of the mixed findings for maternal age, we are unable to conclude whether age is a risk factor for PP or not, and thus it is characterized as inconsistent.

Labour and obstetric complications

Labour and obstetric complications are examined in 7 studies with mixed findings with regard to their association to the development of PP. Agrawal et al. (1990) carried out a prospective cohort study in India and found no significant associations between physical perinatal complications and development of PP. McNeil (1988) found no significant differences between women who developed PP and women who remained well postpartum and any obstetric or delivery variable. Null findings were also reported in Vikström et al. (2017) and Meltzer-Brody et al. (2017), who both found a lack of significant associations between pregnancy and delivery complications

and risk of PP. A retrospective cohort study by Blackmore et al. (2006) reported mixed significance for labour and obstetric variables. They found no significant association between pregnancy complications and development of PP (OR; 1.01, CI; 0.31-3.33, $P = 0.988$) but did report a significant association between delivery complications and development of PP (OR; 2.68, CI; 1.15-6.25, $P < 0.022$). Other significant findings come from Nager et al. (2008), who found significant differences between women who developed PP and those who remained well in the following obstetric variables: respiratory disorder in neonate ($P = 0.001$), severe birth asphyxia ($P = 0.039$), preterm birth ($P < 0.001$), perinatal death ($p = 0.028$), and small for gestational age infant ($P < 0.001$). However, after controlling for hospitalisation for psychiatric disorder within 2 years before delivery, only preterm birth remained significant. Additionally, Upadhyaya et al. (2014) reported maternal complications during the perinatal period as significantly associated with PP ($P = 0.01$). Considering these mixed findings, we are unable to conclude whether or not labour and obstetric act as a risk factor for PP, and thus this factor is categorized as inconsistent.

Negative life events

A total of 7 studies investigated the association between severe and negative life events and PP, yielding mixed findings. A longitudinal cohort study by McNeil (1988) investigated the effects of situational life problems and interpersonal problems such as relationship problems, housing problems, and financial difficulties on PP and found no significant difference between women who developed PP and women who remained well postpartum. Dowlathshahi (1990) conducted a retrospective interview study of 66 women and found the rate of stressful or major objective negative events did not significantly differ between those with PP and controls. Warselius et al. (2019) specifically investigated whether the recent death of a close relative was associated with PP in women with or without a history of psychiatric disorder and found no association between PP death of a close relative (HR; 0.96, 95% CI; 0.74-1.25). Additionally, no significant associations were found for timing of loss, cause of death, or relationship to deceased. A prospective study by Marks et al. (1991) found that the rate of severe life events for women with PP was raised but not at a significant level ($P = 0.16$). However, Kumar et al. (1993) did find a significant difference in the presence of marked/severe life events between high-risk women who relapsed postpartum, high-risk women, and controls who remained well ($P < 0.05$). Additionally, a recent cross-sectional study by Aas et al. (2020) found that women with PP reported more recent stressful life events compared to controls and they had significantly higher scores of perceived stress than healthy controls ($P = 0.007$). Due to the mixed observations relating to negative life events, we are unable to consider this a risk factor for PP, and thus it is categorized as inconsistent.

Education

Several studies included observations on the effects of education on PP with mixed findings. Kirpinar et al. (1999) conducted a retrospective cohort design with matched controls and found that, among Turkish women with first time admission for psychosis and controls, the level of education of the women with PP was significantly lower than controls ($P < 0.05$). Hellerstedt et al. (2013) found the inverse, reporting that higher levels of education were associated with PP. They found that women with more than 9 years of education had two-fold higher odds of postpartum hospitalisation ($OR = 2.05$ $CI = 1.16-3.62$, $P = 0.014$). Three other studies failed to identify any significant differences in education levels and development of PP (Nager et al. 2006; Upadhyaya et al. 2014; Nager et al. 2005). Overall, the findings with regard to education are mixed, and thus we cannot conclude that this is a risk factor for PP.

Living with father of the child

A total of three studies investigated the association between living with the father of the child and the development of PP with mixed findings. Two studies identified a lack of significant association between co-habiting with the father of the child and developing PP. In a nationwide register-based study, Hellerstedt et al. (2013) found no significant difference in the risk of PP for women not co-habiting with the father of their infant compared to women who did. Nager et al. (2006) similarly found that not living with the father did not significantly increase the risk of PP, despite an earlier study by Nager et al. (2005) reporting higher risk of PP for mothers not living with the father of the child. Overall, the findings are mixed, and thus we cannot consider co-habiting with the father of the child or not as a risk factor and instead categorize it as inconsistent.

Sex of child

Sex of the child has been investigated as a risk factor in three studies with mixed findings. Blackmore et al. (2006) carried out a retrospective cohort study and reported an association between gender of the baby and development of PP, although this result was not significant ($P = 0.107$). Similarly, Mighton et al. (2016) found a non-significant trend towards a higher risk for PP among women with female babies. Agrawal et al. (1990) did, however, find significant results, reporting a significant relationship between birth of a female child and puerperal psychosis among a cohort of 144 Indian women. Overall, these findings suggest a potential trend towards higher risk for PP among female births but, due to the lack of significance found in Mighton and Blackmore, we consider these findings inconsistent and thus cannot consider sex of the child as a risk factor for PP.

Socioeconomic factors

Socioeconomic factors were investigated in three studies with mixed findings. A longitudinal cohort study by McNeil (1987) found no significant difference between cases of PP and controls who remained well regarding social class. However, two studies did identify significant results between socioeconomic variables and development of PP. Nager et al. (2006) found that women living in the poorest neighbourhoods exhibited significantly higher risk for first time hospitalisation for PP ($HR; 1.49$ ($95\% CI; 1.15-2.91$, $P = 0.002$)). Upadhyaya et al. (2014) found that lower per-capita income was significantly associated with PP ($P = 0.018$). Overall, the findings are mixed, and the ratio of positive to negative findings is insufficient to consider socioeconomic factors as risk factors for PP.

Discussion

This is the first systematic review to synthesize the quantitative research on risk factors for PP. The review aimed to identify any factors which meaningfully increase the risk of developing PP that can be used to inform future interventions. This review conducted a systematic search of existing literature and identified a wide range of factors as potential risk factors for PP. Any factors with three or more observations were considered to have sufficient evidence in order to be considered in this review, based on the criteria used by Hölzel et al., (2011) in a systematic review of risk factors for chronic depression. For a factor to be considered consistent the number of positive to negative findings had to be a ratio of 4:1 or more. A total of 4 factors were identified that yielded consistent results across observations, according to these criteria: personal history of psychosis or related psychiatric disorders, severity and recency of prior psychiatric illness, marital status, and type of delivery. A history of psychosis or related disorders and severity and recency of prior bouts of illness were both considered consistent risk factors for the development of PP with all studies investigating these factors finding a significant relationship with PP. Marital status was consistently found to lack any significant association with PP and is thus not considered a risk factor. Type of delivery was also categorised as consistent with the ratio of non-significant to significant findings 5:2 and is thus not considered to be a risk factor for PP. The remaining factors that had sufficient observations to be discussed yielded mixed findings and are thus inconclusive at the present. The findings of this review confirm that a psychiatric history of psychosis is an important risk factor for the development of PP. The finding that severity and recency of psychiatric illness are significant and consistent risk factors for PP is novel and has not been explored in any prior reviews. The inconsistency of other risk factors highlights the complex aetiology of the disorder.

This review failed to identify consistently significant findings for factors that are typically considered to increase risk of

PP, namely parity and labour and obstetric complications. In the case of labour and obstetric complications, the National Health Service states that, although the cause of PP is not known, women are more at risk if they experience "a traumatic birth or pregnancy." However, this review did not find evidence to support these claims, with 5 out of the 8 observations relating to labour and obstetric complications failing to find any significant associations with increased risk of PP. This disparity highlights that, in the instance of PP, NHS claims do not reflect primary literature. Additionally, this review did not find that primiparity (or first childbirth) is a consistent risk factor for PP with 3 observations failing to find significance and 4 observations reporting significant associations between parity and PP. Despite the lack of consistent association found between parity and PP, there are several studies in this review that selected primiparous women only on the assumption that primiparous women differed significantly in their risk for PP than non-primiparous women (Mighton et al. 2015; Nager et al. 2005; Harlow et al. 2007; Meltzer-Brody et al. 2017; Hellerstedt et al. 2013; Valdimarsdottir et al. 2009; Vikstrom et al. 2017). This assumption is commonly held, despite a lack of consistent evidence, possibly due to more commonly-cited cohort studies reporting an association (e.g. Kendell et al. 1981). Although parity and labour and obstetric complications are often identified as risk factors for PP, there was not sufficient evidence found to support these claims in this systematic search. This may reflect the underlying complex aetiology of PP and the relative lack of understanding held about the disorder, compared to other postpartum conditions such as postpartum depression (PPD).

The lack of consistent findings found for the majority of factors assessed in this review may reflect an underlying complex aetiology of PP or may reflect inconsistencies in the identification of PP or differences in recruited populations in the literature. A limitation of this study is the differences in recruited populations and the inclusion of studies that measure PP across different cultural groups. These inconsistencies across studies may impact the generalisability of these results. Davies (2017) argues that there are numerous features of PP, particularly its low prevalence, heterogeneity, and unpredictability, that make understanding its aetiology and pathophysiology challenging. There remains ongoing debate in the field as to the classification of PP. Some regard the illness as the postpartum presentation of an existing underlying disorder that lies within the bipolar spectrum and others consider it as a distinct entity in itself (Pfuhmann et al., 2002). At present, there is no official Diagnostic and Statistical Manual (DSM) or International Classification of Diseases (ICD) code for postpartum psychosis, and women experiencing psychotic symptoms postpartum may instead be characterised under a variety of related terms. The 10th edition of ICD (WHO, 1993) recommends that women experiencing these symptoms are classified by the form of the illness, without reference to the postpartum onset. A further category F53.1 of "severe mental and behaviour disorders associated with the puerperium"

can also be used in instances where it is not possible to diagnose the mother with some variety of schizophrenia or affective disorder. The 5th edition of DSM (American Psychiatric Association, 2013) allows episodes of mania, hypomania, or major depression to be qualified by the use of "peripartum onset specifier" in cases where symptoms present during pregnancy or the first four weeks of the puerperium.

The failure of diagnostic manuals to recognise PP as a complex disorder occurring after childbirth presents problems for clinicians, epidemiologists, and researchers. For example, there is a wide variety of assessments and definitions used in the literature to identify women suffering with PP as well as a lack of consistency in timeframes used to assess PP (Vander-Kruik et al. 2017). The widest time frame considered to reflect PP in this study was within one year of delivery (Lewkowitz et al. 2019; Lewkowitz et al. 2020; Brown et al. 2019; Vikström et al. 2017) and the narrowest time frame was within four weeks of delivery (Blackmore et al. 2006). This highlights the lack of consistent time frame used when assessing PP in the literature. By definition, PP occurs rapidly in the postpartum period (Sit et al. 2006). This is reflected in the DSM-5 specifier "with peripartum onset" which can be applied in instances where symptoms occur during pregnancy or within the 4 weeks following delivery. However, several studies in this review consider PP as occurring well beyond this timeframe, raising the issue as to whether or not they were measuring true cases of PP. Such methodological variation prevents researchers from obtaining accurate estimations of prevalence and makes direct comparison between studies difficult. In order for accurate assessments of prevalence and risk to take place, we must first come to an accepted definition and timeframe for PP in the literature.

Some key strengths of this systematic review are its comprehensive search strategy with 965 papers screened, the use of two reviewers at the screening stage, use of quality assessment, and the broad inclusion criteria. However, there are some methodological limitations of this review that are important to consider when drawing conclusions from this study. First, no meta-analyses were conducted due to the heterogeneity of study types, designs, measures, and the lack of consistent definition of PP. This limits the strength of conclusions able to be drawn. Additionally, this systematic review conducted a search of literature published with no exclusion based on date published. This is in contrast to the WHO systematic review guidelines which suggest including literature within the past 15 years only. The choice was made to not generate exclusion criteria based on date of publishing due to the fact that this would have excluded a number of rigorously conducted studies that were conducted prior to this date such as Allwood et al. (2000), Kendell et al. (1987), and Kiprinar et al. (1999). There was also no grey literature search carried out, which limits the scope of this search. This review uses criteria set out in Hölzel et al. (2011), which categorises evidence as insufficient if less than three observations for a single characteristic are considered in the review, as set out in the methods. This

method allows for the simplification of decisions around evidence synthesis. However, it may obscure good research and give credence to poor research done multiple times. However, this possibility was mediated by the exclusion of any studies rated as low in methodological quality, according to the Critical Appraisal Skills Programme of the British National Health Service.

The results of this study have important implications for treatment and early intervention for PP. The National Health Service in the United Kingdom has developed several perinatal mental health care pathways, and the need for appropriate and timely interventions has been identified. Pathways of care are currently divided into primary prevention strategies (preconception advice), secondary prevention (early assessment and treatment), and acute phase interventions (inpatient care) (NHS, 2018). Preconception advice aims to prevent avoidable mental health problems and minimise the risks associated with pregnancy. Specialist assessment aims to improve identification and reduce the number of adverse outcomes associated with undiagnosed and untreated mental health problems. Emergency assessment supports women who may require urgency or emergency attention in situations where the mother and baby may be at risk. Psychological intervention is recommended for a range of perinatal mental health issues. Inpatient care is necessary for women with severe or complex mental health needs, typically in the form of a Mother and Baby Unit (MBU). The identification of risk factors may also allow for further development of preventative treatment which may prevent the illness from developing or reduce the severity and distress of the mother. However, due to the inconclusivity of many factors identified in this review, more research is needed to illuminate whether any of the factors determined as inconsistent in this study definitively act as risk factors or not. Research methodology should be rigorous and ensure a large sample in order to increase generalisability.

Conclusion

The identification of previous history of psychosis or related disorders and severity and recency of prior psychiatric illness as reliable risk factors for PP offer important clinical implications. Both of these variables are identifiable prenatally, and thus interventions that seek to reduce development and severity of PP can begin before delivery. Women who are identified as having a psychiatric history of psychosis or related disorders such as bipolar disorder should be considered at risk for PP and, according to the NHS, should have a pre-birth planning meeting with everyone involved in their care to explain how to get help quickly if they become ill and strategies to reduce their risk of becoming ill (*Postpartum Psychosis – NHS n.d.*). At-risk women may benefit from consultations with a psychiatrist pre-delivery to be informed of symptoms to recognise after birth and discuss possible treatment options after delivery to avoid the manifestation of PP (Yonkers et al., 2004). If symptoms of PP do manifest, early intervention is

crucial (Doucet et al., 2011). Given the severity of PP, pharmacological treatment and inpatient care, preferably in a Mother and Baby Unit, are typically always required (NICE 2018, Jones and Smith 2009). This review also reports that characteristics of previous incidences of psychiatric illness, namely illness recency and severity, is a consistent risk factor for PP. This finding has potential implications for the development of new interventions and suggests that women at the highest risk for PP are those with a more recent, longer admission for a psychotic or related disorder. Such women may be an important target for pre-delivery support and increased monitoring in the early postpartum period.

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Appendix

Appendix 1

Summary of all studies

Authors (year), place, sample size	Risk factors measured	Diagnosis of PP	Study design	Findings
McNeil (1986), Sweden, n = 192	Personal history of psychosis	Psychiatric records, severity of disturbance by senior project diagnostician, occurrence of illness up to 6 months postpartum	Longitudinal cohort study with matched controls	Significant difference in rates of PP among subjects with a history of psychosis and controls
McNeil (1987), Sweden, n = 151	Characteristics of previous psychiatric illness, socioeconomic status, parity, age, marital status	Psychiatric records, occurrence of illness up to 6 months postpartum	Longitudinal cohort study with matched controls	Significant association between duration, severity, and recency of previous psychiatric illness with PP. No significant difference between women with PP and controls in parity, social class, age, or marital status
McNeil (1988), Sweden, n = 151	Familial and life-situational characteristics, interpersonal problems and relatives' attitudes towards pregnancy, maternal attitude toward pregnancy, symptoms, and experienced health during pregnancy	Psychiatric records, occurrence of illness up to 6 months postpartum	Longitudinal cohort study with matched controls	No significant difference between women with PP and controls in interpersonal difficulties, support, familial attitude towards pregnancy, maternal somatic health. PP cases reported more preparation for the child and a more positive attitude toward the pregnancy
McNeil (1988), Sweden, n = 151	Psychosocial characteristics of labour and delivery: maternal anxiety, control over own behaviour, midwife help, attendance of husband, response to infant	Psychiatric records, occurrence of illness up to 6 months postpartum	Longitudinal cohort study with matched controls	Later onset cases of PP (>3 weeks) reported significantly more anxiety, less control, less midwife help, and less frequent attendance from husband compared to no PP controls. No statistically significant difference was found between PP and non-PP cases on any labour or delivery variable or response to infant
McNeil (1988), Sweden, n = 151	Maternal mental health characteristics during pregnancy: depression, denial, irresponsibility, delivery-based fears, disturbance, excitement	Psychiatric records, occurrence of illness up to 6 months postpartum	Longitudinal cohort study with matched controls	Among cases of PP there was a non-significant trend of less depression and significantly fewer delivery-based fears. Significantly more excitement and disturbance in later pregnancy was reported and no significant trends or more irresponsibility and denial tendency
McNeil (1988), Sweden, n = 84	Labour and obstetric complications, offspring abnormalities	Psychiatric records, occurrence of illness up to 6 months postpartum	Longitudinal cohort study with matched controls	No significant differences between women with PP and controls in any labour or obstetric factor or offspring abnormality. A non-significant trend was observed for induction of labour among early onset cases of PP compared to controls
Morris (2020), Canada, n = 365	Folate levels, MTHFR C677T genotype	Administration of Clinician-Administered Rating Scale for Mania (CARS-M) and the	Prospective longitudinal cohort study	No significant interaction between MTHFR genotype and RBC folate level on the probability of meeting psychotic symptom

		Positive and Negative Symptom Scale (PANSS). 5 items of PANSS assess psychosis		criteria on the PANSS
Meltzer-Brody (2018), Denmark, n = 129,439	Adverse childhood experiences	Psychiatric records linked with National birth registry, occurrence of illness up to 6 months postpartum	Nation-wide register-based cohort study	Across all studies adverse childhood experiences including family disruption, parental criminality and parental death, there was no increased risk of PP
Allwood (2000), South Africa, n = 314 (retrospective study) n = 165	Personal history of psychosis, family history of psychiatric illness, parity, stressful life event	Psychiatric records and additional scales, occurrence of illness within 3 months of delivery	Retrospective and prospective cohort study with matched controls	Significantly higher incidence of psychiatric history, family psychiatric history and perceived stress in cases of PP compared to controls. No difference in number of past pregnancies
Nager (2005), Sweden, n = 502,767	Sociodemographic characteristics: age, education level, co-habitation with father of child,	First hospital admission due to psychotic disorder within 3 months postpartum	Nation-wide register-based cohort study	Older age and not co-habiting with the father increased the risk for PP. Education level was not associated with PP
Hellerstedt (2013), Sweden, n = 1842	Characteristics of previous psychiatric illness, age, education, labour, and obstetric complications	Psychiatric records, occurrence of illness within 90 days of delivery	Nation-wide register-based cohort study	More recent, longer-term, and multiple pre-conception psychiatric hospitalisations were independently significantly associated with PP. No significant differences found in age, education, or pregnancy complications between groups
Lewkowitz (2020), USA, n = 1,076,245	Twin delivery	Psychiatric records, emergency department encounter or inpatient admission within 1 year of deliver	Retrospective cohort design	The risk for PP was comparable among women delivery singletons and twins
Lewkowitz (2019), USA, n = 1,203,050	Still birth	Psychiatric records, emergency department encounter or inpatient admission within 1 year of delivery	Retrospective cohort design	The risk of PP was significantly higher after still-birth compared to live-birth
Di Florio (2018), UK, n = 887	Personal history of psychosis, characteristics of previous psychiatric illness	Psychosis was defined as an episode of DSM-IV mania, psychotic depression, or mixed episode within 6 months of delivery	Retrospective cohort design	Women with a history of perinatal affective psychosis were six times more likely to develop PP re-occurrence. A statistically significant association between PP and number of episodes per year of psychiatric illness
Aas (2020), UK, n = 30	Stress response, stressful life events	Clinical interviews for DSM-IV Axis I Disorders and Positive and Negative Syndrome Scale (PANSS)	Cross-sectional design	Women with PP reported significantly more recent stressful life events than controls and had significantly higher scores of perceived stress. (We did not consider biological stress markers in this review as these measurements did not precede PP and thus give no indication of directionality)
Brown (2019), Canada, n = 858,004	Chronic physical health conditions	Diagnosis captured by visit to GP, psychiatrist, emergency department or hospitalisation with diagnosis of psychotic disorder. Illness occurrence within 365 days of delivery	Population-based retrospective cohort design	PP was significantly more likely to occur in women with chronic physical disorders than women without
Mighton (2016), Canada, n = 60	Personal history of major depressive disorder (MDD), sex of baby	Psychosis defined using five items from PANSS administered during pregnancy and at 1 week, 1 month and 3 months postpartum	Prospective longitudinal cohort study	23% of women with MDD scored above threshold for psychosis at one or more time-points, suggesting elevated risk. Non-significant trend towards higher symptoms on PANSS among mothers of girls.

Sharma (2004), UK and Canada, n = 42	Duration of labour, sleep disruption, age, personal history of psychiatric illness	Hospital diagnosis of puerperal psychosis	Retrospective chart review	Women with PP had a significantly higher number of night-time deliveries and experienced significantly longer labour than controls. Mean age was not statistically different between groups. The majority of women with PP suffered from bipolar or schizoaffective disorder
Marks (1992), UK, n = 88	Personal history of psychiatric illness, characteristics of previous psychiatric illness, age, parity, social class, marital status, duration of marriage, lack of a confidant, unplanned pregnancy, early separation from mother or father and unemployment.	Assessment by psychiatrist based on interview, case notes and Schedule for Affective Disorder and Schizophrenia (SADS). Illness occurrence within 6 months postpartum	Prospective cohort design	Those who became psychotic postpartum had more recently been admitted compared to non-psychotic cases. The variables age, parity, social class, marital status, duration of marriage, lack of a confidant, unplanned pregnancy, early separation from mother or father and being unemployed were not associated with relapse. None of the women with a history of MDD were categorised as psychotic after their delivery. 46% of the women with psychotic symptoms postpartum had a previous diagnosis of bipolar or schizoaffective
Agrawal (1990), India, n = 144	Sex of baby, pregnancy, or postpartum complications	Diagnosed according to Research Diagnostic Criteria (RDC). Illness occurrence within 3 months of delivery	Prospective cohort design	No significant associations found between perinatal physical complications and PP. Significant relationship found between birth of a female child and puerperal psychoses
Upadhyaya (2014), India, n = 100	Pregnancy and obstetric complications, age, education, income, family history of psychiatric illness, marital status	Patients admitted for psychiatric care and diagnosed with psychotic symptoms by a consultant psychiatrist using DSM IV-TR). Illness onset within 42 days of delivery.	Cross-sectional case control study	Education and family history of psychiatric illness were not significantly associated with PP. Lower age and lower per-capita income were significantly associated with PP and presence of husband differed significantly between cases of PP and controls. Maternal perinatal complications, new-born complications and primiparity were significantly associated with PP and type of delivery and complications in pregnancy were not.
Kendell (1981), UK, n = 704	Parity, type of delivery, marital status	Psychiatric records for all psychiatric admissions for psychosis up to 90 days postpartum	Population-based cohort design	Primiparity and caesarean section were significantly associated with PP. No significant relationship was observed for marital status and PP
Kendell (1987), UK, n = 385	Parity, type of delivery, marital status, perinatal death	Psychiatric records for all psychiatric admissions for psychosis up to 90 days postpartum	Population-based cohort design	Primiparity was associated with a heightened risk for PP and each psychoses sub-group showed a significant excess of mothers with no living children. No significant associations were observed for marital status, type of delivery or perinatal death and PP
Kirpinar (1999), Turkey, n = 128	Age, education, family history of psychiatric illness	Psychiatric records and re-diagnosis according to DSM-IV by one of the authors	Retrospective cohort design with matched controls	The level of education was significantly lower in women with PP. No significant differences between PP group and controls with regard to positive family history of psychiatric disorders or mean age
Valdimarsdottir (2009), Sweden, n = 745,596	Age, birth weight, type of delivery	Psychiatric records from Hospital Discharge Registry for psychosis during the first 90 days postpartum	Nation-wide register-based cohort study	The risk of PP was independently affected by maternal age. High birth weight is associated with reduced risk and caesarean delivery was not significant as a risk factor

Vikstrom (2017), Sweden, n = 29,036	IVF, history of psychiatric illness, type of delivery, age, marital status, education	Psychiatric diagnosis from ICD-10 limited to 1 year postpartum. ICD codes for schizophrenia, schizotypal and delusional disorders, manic episode and bipolar disorder and severe mental and behavioural disorders associated with the puerperium	Nation-wide register-based cohort study	No significant differences were found in PP prevalence among women who underwent IVF compared to controls. No significant associations were found for pregnancy or delivery complications, type of delivery, age, marital status, or education for PP. The risk of PP was increased in women with a history of any psychiatric disorder as well as in women with a psychotic disorder, bipolar disorder, anxiety disorder, depression, or personality disorder separately
Harlow (2007), Sweden, n = 612,306	Characteristics of previous psychiatric illness	Psychotic admissions based on ICD-8, ICD-9 and ICD-10 for schizophrenia, schizoaffective disorders, and other non-affective psychoses	Nation-wide register-based cohort study	An increased risk for PP was observed for more recent psychiatric hospitalisations, more hospitalisation stays and longer length of the most recent stay
Dowlatsahi (1990), UK, n = 66	Stress and negative life events	Patients admitted to hospital for psychoses within one month of delivery	Retrospective interview study	No significant differences were found in mean number of life events or major objective negative events in women with PP and controls
Marks (1991), London, n = 88	Negative life events	Psychiatric case notes and Schedule for Affective Disorder and Schizophrenia (SADS) interviews at six months postpartum	Prospective study	The rate of severe life events for women with PP was raised but not significantly higher. All episodes of PP were among women with a prior history of bipolar or schizoaffective disorder although this was not examined statistically
Warselius (2019), Sweden n = 5,246,97	Negative life events	Psychiatric records (typically diagnosis was based on psychiatrists using DSM), illness onset within 90 days	Nation-wide register-based cohort study	Recent death of a close relative was not associated with PP in women with and without a history of psychiatric disorders. Additionally, there was no association between PP and timing of loss, cause of death or relationship to the deceased
Nager (2006), Sweden, n = 485,199	Education, age, co-habitation with father, socioeconomic factors	Hospital admission due to psychotic disorder within three months of delivery	National population-based cohort study	Women living in the poorest neighbourhoods exhibited significantly higher risk of PP. Lower years in education and not living with the factor did not significantly increase the risk for PP. Higher age ranges (40-44) were also associated with higher risk of PP compared to ages 20-24.
Kumar (1993), UK, n = 81	Negative /stressful life events, neuroendocrine levels	Psychiatric diagnoses based on subject interviews at 6 months postpartum using the Schedule for Affective Disorder and Schizophrenia (SADS) and hospital case notes	Prospective cohort design	There was a significant difference in marked/severe life events between the high-risk women with PP and high-risk women who remained well and controls who remained well. Women with PP had higher GH responses to APO than either women who remained well or controls
Nager (2008), Sweden, n = 1,133,368	Obstetric and pregnancy complications, type of delivery	Psychiatric hospitalisation due to psychotic within 3 months after delivery	National population-based cohort study	There was a significant difference in rates of PP among women who had caesarean section and those who did not. Significant differences in rates of PP in exposure to the following obstetric variables; respiratory disorder in neonate, severe birth asphyxia, preterm birth, perinatal death, small for gestational age infant. However, after adjustment for hospitalisation for psychiatric disorder within 2 years before disorder, only preterm birth remained significant

Blackmore (2006), UK, n = 129	Type of delivery, parity, obstetric and pregnancy complications, sex of baby	Interviews by a trained psychologist or psychiatrist using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) and case notes within 4 weeks of delivery	Retrospective cohort design	No significant associations with developing PP were found for caesarean section, gestation period, gender of baby or pregnancy complications. Significant association were found for delivery complications and primiparity for PP
Meltzer-Brody (2018), Denmark, n = 392,458	Obstetric and pregnancy complications, socioeconomic factors	Psychiatric records, onset within the first 12 months postpartum	Population- based cohort design	No significant associations between socio- economic factors, obstetric complications or pregnancy complications and risk of PP

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Hannah Netschytailo graduated from the University of North Carolina at Chapel Hill in May 2021 with a bachelor's degree in Psychology with highest honors and Human Development and Family Studies. As an undergraduate, Hannah worked as a research assistant in Dr. Eva Telzer's Developmental Social Neuroscience Lab and Dr. Keely Muscatell's Social Neuroscience and Health Lab. She currently works as a research assistant under Dr. Desiree Murray at the UNC Center for Health Promotion and Disease Prevention, assisting in various studies that focus on promoting positive youth development. She plans to apply to Clinical Psychology Ph.D. programs in hopes of furthering her studies on youth experiencing adversity and behavioral disorders.



Was there a particular experience that sparked your research interests?

Growing up in a rural, low-income area, I always wondered why some of my peers exhibited resiliency and thrived amongst adversity while others experienced behavioral issues and negative outcomes. I wanted to understand what factors are protective against the development of maladaptive behaviors during youth, whether that be supportive relationships with family and friends, individual well-being, or certain school or neighborhood environments. As an undergraduate, I was given the opportunity to explore these questions through two independent research projects (one including my honors thesis) and really developed a passion for wanting to improve the lives of youth. In the future, I hope to further my research and pursue a Ph.D. in clinical psychology.

Who has been the most influential person in your life?

It's impossible to narrow down a single, most influential person as I've been fortunate to have several people make an impact on my life and academic career. I'm grateful for several people: my parents and siblings for teaching me kindness and perseverance; my friends and partner for always providing me with happiness, jokes, and motivation;

my research mentor, Dr. Natasha Duell, for being a source of ongoing encouragement and moral support in my academic endeavors; and finally, the various individuals I've had the opportunity to work with in a lab setting for giving me the tools to pursue my research interests.

What is your greatest accomplishment?

Being the first person in my family to graduate with a four-year degree has definitely been my greatest accomplishment so far. It's difficult to go into college without being able to ask your parents about their experiences and having to navigate the invisible rules of academia without ever knowing there were rules in the first place. However, with the support of several individuals inside and outside of UNC, I was able to reach my goal of graduating with a bachelor's degree and prove to myself that I am capable of achieving my dreams.

Where do you see yourself in 10 years?

In 10 years, I hope to have a Ph.D. in clinical psychology and be actively contributing to research in the field. I also hope to mentor students and provide them with the same support I've been given. Besides that, I am open to the various paths a Ph.D. in clinical psychology can take me. Overall, I just hope I'm happy and making a positive impact!

How Adolescents' Resiliency Mitigates the Relation Between Household Dysfunction and Maladaptive Behavior

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Adverse childhood experiences (ACEs), such as household dysfunction, impact adolescents' externalizing and internalizing behaviors. However, personal and interpersonal resilience factors may buffer the effects of ACEs on adolescent psychopathology. The present study explored how specific resilience factors (i.e., personal well-being, family connectedness, and peer connectedness) prospectively buffered against the negative effects of household dysfunction on externalizing and internalizing behaviors. Household dysfunction was measured by assessing parental incarceration, substance use, mental illness, and marital status. Participants (52% female) included 176 adolescents with various racial and ethnic identities (White = 30%, Black = 23%, Hispanic/Latino = 35%, Multi-Racial = 9%, and 3% other racial/ethnic identities) aged 11-14 years old during the first wave of data collection and 12-15 years old during the second wave. Results indicated that household dysfunction served as a risk factor for adolescent externalizing behaviors at extremely low levels of family connectedness. Furthermore, this finding suggests that higher levels of family connectedness may be protective as these levels did not possess a significant association between household dysfunction and externalizing behaviors. However, peer connectedness and well-being were not shown to be protective against externalizing and internalizing behaviors. Per these results, prevention and intervention methods for adolescent externalizing behaviors may be most successful when focusing on improving connections within the family.

Keywords: adolescence, adverse childhood experiences, household dysfunction, maladaptive behavior, resilience

Over two decades of research stemming from the Adverse Childhood Experiences study (Felitti et al., 1998) has demonstrated an association between adverse childhood experiences (ACEs) and the development of maladaptive behaviors, such as delinquency and inhibition (Quinn et al., 2019), that have lasting negative impacts on development. Adversity can impact adolescents in various contexts, including in their neighborhood and within the home. The household and family environment, however, is particularly important when studying adolescent behavior. Children develop coping mechanisms by observing their caregivers' behaviors and reacting to the emotional climate of family members (Shapero & Steinberg, 2013). Furthermore, dysfunction and stress felt within the household context results in behavioral issues during adolescence (Racine et al., 2020). Despite these risk factors, interpersonal and individual strengths may buffer against the negative effects of ACEs on adolescent psychopathology (Shapero & Steinberg, 2013). Of particular interest are the ways in which adolescents'

connections and their own well-being protect them from the effects of adverse experiences in childhood. In this paper, the impact of household dysfunction on adolescent maladaptive behavior and the protective nature of personal well-being and connections with family and friends will be discussed.

Adolescence is an important developmental period during which to study the effects of household dysfunction on psychopathology, given the well-documented increase in externalizing and internalizing behaviors during the second decade of life (Barzeva et al., 2019; Steinberg, 2008). Externalizing behaviors are those that are directed towards one's environment and include disruptive and delinquent acts, such as fighting, rule-breaking, impulsivity, and inattention. Contrastingly, internalizing behaviors are those that are directed towards oneself, and include inhibition and withdrawal actions, such as self-harm, poor concentration, feelings of sadness, and avoiding others (Willner et al., 2016). Given the heightened significance of interpersonal relationships during adolescence (Barzeva

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et al., 2019), connectedness with family members and peers may be particularly effective in mitigating the consequences of a negative household environment. Despite this, most prior research has explored the effects of childhood experiences on adolescent functioning or has asked adults to retrospectively report on their adolescence. To this end, the present study aimed to address this gap in the literature by examining whether well-being and connectedness with family and peers mitigated the prospective association between household dysfunction and adolescent externalizing and internalizing behaviors.

Adverse Childhood Experiences

Prior research has identified ten common adverse childhood experiences falling under three distinct categories: abuse (physical, emotional, and sexual), neglect (physical and emotional), and household dysfunction (parent mental illness, incarceration of a relative, violent treatment of the mother, parent substance use, and parent divorce) (Felitti et al., 1998). In the original ACEs study, approximately two thirds of participants experienced at least one ACE, and one fifth experienced at least three ACEs before the age of 18 (CDC, 2020). The prevalence of ACEs increases the risk for negative outcomes, in that individuals with more ACEs are at an increased risk for negative mental and physical health outcomes than their counterparts with fewer ACEs (Sacks & Murphey, 2018).

Household Dysfunction

With aspects of household dysfunction being some of the most prevalent ACEs individuals experience (Sacks & Murphey, 2018), there is a need to study household dysfunction further. Composed of diverse variables within the home environment, household dysfunction includes parent mental illness, the incarceration of a relative, violent treatment towards a mother-figure, parent substance use, and the divorce of one's parents (Felitti et al., 1998). Exploring household functioning is important due to its consistent impact on adolescents' lives, including their self-regulation of behavior (Björkenstam et al., 2016). The specific aspects of household dysfunction within this study and their impact on adolescents' lives will be discussed in the following sections.

Parent Marital Status. As one of the most common ACEs among individuals in the U.S. (Sacks & Murphey, 2018), parental divorce and separation has the potential to negatively impact the behavioral development of a large number of adolescents. Parental divorce and marital issues have been shown to produce intense stress in adolescents' lives, oftentimes resulting in behavioral issues (Taanila et al., 2002). Before the divorce or separation, the family structure may become unclear and adolescents are more likely to be included in their parents' conflict and tensions. Adolescents may sometimes be overlooked or used as a means to win arguments against the other parent, ultimately leading to the development of

coping mechanisms that present behaviorally (Taanila et al., 2002). Kelly (2002) found that adolescents with parents who exhibited high-intensity arguments developed more externalizing behaviors, such as aggression, and internalizing behaviors, such as having poor self-esteem, than their counterparts experiencing low-intensity parental arguments. Furthermore, single parents may have to work long hours due to the financial constraints of a single-income household, leaving adolescents with increased unsupervised time and more opportunities to exhibit delinquent behaviors. For example, Laughlin (2013) found that 31.6% of 12-14 year-olds in single-father homes were left unsupervised regularly, with 7 hours being the average amount of time children were in unsupervised situations each week. Adolescents' delinquent behaviors oftentimes go unpenalized when they are left unsupervised for increased periods of time, leading to the reinforcement of such behaviors (Patterson & Stouthamer-Loeber, 1984). Overall, living in a divorced or single-parent household may increase the risk of adolescents' internalizing and externalizing behaviors, making this aspect of household dysfunction important to study.

Parent Substance Use. Another aspect of household dysfunction that can negatively impact adolescent behavioral development is parent substance use. Research has found that children of parents with substance use disorders were at an increased likelihood for externalizing and internalizing behaviors (Bountress & Chassin, 2015). Furthermore, research has indicated that adolescents with parents who use substances, including cigarettes, alcohol, and marijuana, are more likely to use said substances themselves due to parental modeling or lack of discipline from intoxicated parents (Hops et al., 1996). Adolescents' internalizing behaviors can be impacted by their own substance use, since substances may impact mental well-being (Hassan & Ali, 2011) and exacerbate the symptoms of present affective disorders (Quello et al., 2005). Additionally, being under the influence of substances may alter adolescents' behavior, leading to engagement in delinquent and externalizing behaviors (D'Amico et al., 2008). For example, D'Amico et al. (2008) found that adolescents who used substances were more likely to engage in delinquent behavior, such as fighting and vandalism, in the future.

Parent Depression. As substance use oftentimes coincides with mental illness, it is important to explore how parent depression impacts adolescent behavior as well. Previous research has suggested that the quality of one's parenting may also become impaired when experiencing depression (Rutter, 1990; Hanington et al., 2010). Thus, children may develop strained relationships with their depressed parent or experience a lack of guidance from a parental figure, potentially impacting how they behave. Furthermore, having a depressed parent can create stress in adolescents' lives due to a lack of parental consistency, warmth, and responsiveness that may occur as a result of the depression (Langrock et al., 2002). The stress that adolescents subsequently feel puts them at risk for developing behavioral issues as a means to cope, including

externalizing and internalizing behaviors. For example, Langrock et al. (2002) found that children of parents with depression exhibited higher rates of aggressive, anxious, and depressive behaviors than children without depressed parents. Additionally, past studies have suggested that characteristics of depression may be passed genetically from parent to child (Hanington et al., 2010). As a result, it is possible that internalizing behaviors may be more prevalent among adolescents with depressed parents than their counterparts with parents not possessing a mental illness.

Parent Incarceration. Another aspect of household dysfunction that has been shown to impact adolescent behavior is the incarceration of a parent. Not only do children of incarcerated individuals oftentimes feel abandoned by and separated from their parents, but they also usually experience stigma and negative financial implications from this parental absence (Aaron & Dallaire, 2010). Furthermore, they may have been exposed to their parents' illegal behaviors or have had increased unsupervised time due to their parents being away, increasing the opportunity for delinquent behaviors to occur (Aaron & Dallaire, 2010). Compared to their peers without an incarcerated parent, adolescents with an incarcerated parent exhibited more externalizing behaviors such as being "disobedient at home" and threatening others, and internalizing behaviors such as being "self-conscious or easily embarrassed" and worrying (Boch et al., 2019). Overall, prior research shows that aspects of household dysfunction negatively impact adolescents' lives and behavior, making it an imperative topic to explore.

Behavior During Adolescence

In general, adolescents become more likely to engage in risky behaviors and develop mental illnesses as a result of neural changes in areas such as the prefrontal cortex, the area responsible for inhibition and decision-making, during puberty (Selemon, 2013). Thus, externalizing and internalizing behaviors may significantly increase during adolescence, making this an important period of development during which to study psychopathology. Negative consequences can result from these behaviors, including incarceration, substance use disorders, and decreased academic performance (Odgers et al., 2008). These consequences can have long-term effects; therefore, it is important to contribute to research on lessening the occurrence of externalizing and internalizing behaviors.

Resilience

Resilience factors may mitigate the association between household dysfunction and behavioral issues. These factors can be broadly defined as characteristics that protect individuals from the negative effects of life occurrences (Sagone & De Caroli, 2014).

Family and Peer Connectedness

Developed as part of the Positive Youth Development framework, the 7 C's of resilience cover a broad range of these strengths — including competence, confidence, connection, character, contribution, coping, and control — that may help adolescents thrive despite adversity (Ginsburg, 2020). Although all 7 C's of resilience are impactful for overcoming adversity, connectedness is particularly important to study, as quality and supportive relationships with parents and peers can impact adolescents' behavioral regulation (McCormick et al., 2016; Steinberg, 2001; Brown & Larson, 2009). This impact may be due to the increased neural sensitivity to social relationships that occurs during adolescence (Barzeva et al., 2019; Steinberg, 2008). However, connections between adolescents and their parents and peers may vary in influence. As adolescents age, reliance for support from their parents shifts to their peers (Nickerson & Nagle, 2005). When determining the protectiveness of relationships and support, it is important to consider the different influences of adolescents' parents and peers.

Personal Well-being

Furthermore, individual resilience factors are important for protection from adversity and its effect on behavioral development. Personal resilience factors protect against delinquent behaviors in a cumulative manner, where adolescents who possess more of these factors are less likely to engage in maladaptive behaviors (Smith et al., 1995). For example, past research indicates that high levels of well-being and life satisfaction served as a protective factor for internalizing behaviors (Deković, 1999). Well-being can be broadly defined as the state of having psychological, social, and physical needs met in a way where challenges are able to be overcome (Dodge et al., 2012). Overall, well-being may be protective as it incorporates both physical and psychological health.

Current Study

To explore the impact of individual and social resilience factors on the development of maladaptive behaviors in adolescence, this study examines the buffering effects of well-being and connectedness to one's family and peers against the association between household dysfunction (categorized by parent incarceration, parent depression, parent substance use, and parent divorce) and adolescent externalizing and internalizing behaviors across time. It is hypothesized that adolescents scoring higher on household dysfunction exhibit more externalizing and internalizing behaviors, but only in the context of low well-being and low peer and family connectedness. Support for this hypothesis would indicate that personal and interpersonal resilience factors could protect against the prevalence of externalizing and internalizing behaviors in adolescence, despite possible dysfunction in adolescents' homes.

Methods

Participants

176 participants (52% female) were recruited from middle schools in rural North Carolina as part of a longitudinal study examining adolescent brain development and behavior (NeuroTeen Study, PI: Eva Telzer). Participants were from diverse racial and ethnic backgrounds (White = 30%, Black = 23%, Hispanic/Latino = 35%, Multi-Racial = 9%, and 3% other racial/ethnic identities). In the first wave of data collection, participants ranged in age from 11-14 years old ($M = 12.4$, $SD = .643$). In the second wave of data collection, participants ranged in age from 12-15 years old ($M = 13.7$, $SD = .576$).

Thirty participants did not continue in the second wave of data collection. Listwise deletion was implemented; therefore, individuals who did not participate during the second wave were still included in the final sample population and analyses. Furthermore, independent samples t-tests indicated that participants who did not participate in the second wave did not differ from their peers on any main study variables, suggesting data were missing at random.

Procedure

Procedures were approved by the local Institutional Review Board and parental consent and adolescent assent were obtained. Adolescent participants and a parent or caregiver completed a self-report questionnaire during an in-person session through Qualtrics as part of the larger study, which also included behavioral measures and fMRI. Furthermore, a trained research assistant was present to answer questions and troubleshoot technological issues while surveys were completed. Research assistants did not look at the questionnaires as they were being filled out to provide a sense of privacy. For the current study, only self-report data were used. Data were collected at two different time points separated by approximately one year except for the connectedness and household dysfunction measures, which were only taken at time 1, and the well-being measure, which was only taken at time two.

Measures

To index adolescent externalizing and internalizing behaviors, the Child Behavior Checklist was used because it is one of the most widely used measures of youth emotional and behavioral problems and has demonstrated strong validity across samples (Ebesutani et al., 2010). Household dysfunction was measured using various measures capturing parent depression, incarceration, substance use, and marital status. These items were chosen because they overlapped with the various aspects of family dysfunction outlined by the original ACEs study (Felitti et al., 1998). Finally, well-being and peer and family connectedness were measured as indicators of resilience. Given the methodological constraints of the study, it was not

possible to index all 7 C's of resilience previously described (Ginsburg, 2020). However, it was felt that a general index of well-being would capture positive psychological functioning and resilience more broadly (Sagone & De Caroli, 2014).

Externalizing behaviors. The Child Behavior Checklist (CBCL) externalizing subscale was used to measure adolescent self-reported delinquent and dysfunctional behaviors (Achenbach & Rescorla, 2001). The CBCL externalizing subscale included 32 items ($\alpha = .876$). Adolescent participants reported on a 3-point scale from 0 (*not true*) to 2 (*very true or often true*) regarding how true certain behaviors were for them in the past 6 months (e.g., "*I physically attack people*"). Higher scores indicated greater externalizing behaviors.

Internalizing behaviors. The Child Behavior Checklist (CBCL) internalizing subscale was used to measure adolescent self-reported anxious and withdrawn behaviors, in addition to somatic complaints (Achenbach & Rescorla, 2001). The CBCL internalizing subscale included 30 items ($\alpha = .884$). Adolescent participants reported on a 3-point scale from 0 (*not true*) to 2 (*very true or often true*) regarding how true certain behaviors were for them in the past 6 months (e.g., "*I cry a lot*"). Higher scores indicated greater internalizing symptoms.

Household Dysfunction

A cumulative risk score composed of parent incarceration, parent depression, parent substance use, and parent marital status was created to calculate the level of household dysfunction for each participant at Time 1 of data collection. For each individual variable, a score of 0 or 1 was given based on the parents' questionnaire answers. With parent incarceration, 0 was given if the parent had never been incarcerated, and 1 if the parent had been incarcerated at least once in their life. For parent depression, 0 was given if the parent scored below 12 out of 26 on the Short Mood and Feelings Questionnaire (SMFQ), and 1 if the parent scored 12 or above. This cut-off value was determined by the SMFQ scoring guidelines for identifying depression (Angold et al., 1995). For parent substance use, a score of 0 was given if the parent had never endorsed the use of a substance in the previous year, and 1 if they had used any substance over the past year. Finally, for parent marital status, a score of 0 was given if the parent was married, and 1 if the parent was single. Scores for each of the individual variables were summed to create a score for level of household dysfunction, with scores ranging from 0 (no risk factors endorsed) to 4 (all risk factors endorsed). The average score for household dysfunction was 0.98, indicating a low mean level of household dysfunction among participants.

Parent Incarceration. Parents of adolescent participants self-reported their offending history, including whether they had ever been arrested. Parents reported either 1 (yes) or 2 (no) regarding if they had ever been arrested.

Parent Depression. The SMFQ for depression was used to measure parent-reported symptoms of depression (Thabrew et al., 2018). The SMFQ for depression included 13 items ($\alpha =$

.855). Parents reported on a 3-point scale from 0 (*not true*) to 2 (*true*) regarding their feelings and actions in the past two weeks (e.g., “*I felt miserable or unhappy*”).

Parent Substance Use. A Health Risk Behaviors (HRB) scale was used to measure parents’ reports of the average number of days per year that they used any of the following: e-cigarette, tobacco cigarette, alcohol, marijuana, pharmaceuticals without a prescription, and hard drugs (e.g., meth, heroin, LSD, etc.). Parents reported the frequency of their substance use over the past year on the following scale: 0 days, 1 to 2 days, 3 to 11 days, 1 day per month, 2 to 3 days per month, 1 day per week, 2 days per week, 3 to 4 days per week, 5 to 6 days per week, or every day.

Parent Marital Status. Parents of adolescent participants self-reported their marital status. Parents originally reported on a variety of statuses, such as widowed or divorced. However, the scale was condensed to either 0 (*married*) or 1 (*single*) for analyses. Parents were considered single if they were not romantically involved with anyone, including those with a deceased spouse.

Resilience Factors

Well-Being. Adolescents self-reported their well-being during Time 2 of data collection using a 5-item scale ($\alpha = .877$). Adolescents reported on a 6-point scale from 1 (*never*) to 6 (*everyday*) regarding their feelings in the past month (e.g., “*satisfied*” and “*that your life has a sense of direction or meaning to it*”).

Connectedness. Identical items were used for the Family Identity and Peer Identity measures at Time 1 of data collection. The Family Identity measure was used to determine how connected adolescents felt to their family in general (Hardway & Fuligni, 2006). The Family Identity measure included 3 items ($\alpha = .611$). Adolescents self-reported on a 5-point scale from 1 (*strongly disagree*) to 5 (*strongly agree*) regarding their connectedness to their family (e.g., “*I feel a sense that I personally belong in my family*”).

The Peer Identity measure was used to determine how connected adolescents felt to their friends (Hardway & Fuligni, 2006). The Peer Identity measure possessed 3 items ($\alpha = .559$). Adolescents used a self-report scale from 1 (*strongly disagree*) to 5 (*strongly agree*) to indicate their connectedness to their friends in general (e.g., “*My friends are important to the way I think of myself as a person*”).

Method of Analysis

Moderation analyses were conducted to evaluate the interactive association between resilience factors and household dysfunction with later externalizing and internalizing behaviors. Separate analyses were conducted for each outcome (internalizing and externalizing) and for each moderator (i.e., family connectedness, peer connectedness, and well-being). All analyses adjusted for Time 1 psychopathology (externalizing

or internalizing behaviors), race/ethnicity (with white omitted as the reference category), and gender (with female omitted as the reference category).

The first step of the regression analyses included Time 1 psychopathology (externalizing or internalizing behaviors), race/ethnicity, and gender as covariates. The second step of the analyses included the main effects of resilience factors (personal well-being, family connectedness, and peer connectedness, respectively) and household dysfunction. The final step of the analyses included the interaction between the resilience factors and household dysfunction.

Results

Descriptive Information

Descriptive statistics and correlations are presented in tables 1 and 2, respectively. An independent samples t-test was conducted to evaluate gender differences in externalizing and internalizing behaviors. Externalizing behavior scores did not significantly differ between males ($M = 43.52$, $SD = 11.34$) and females ($M = 45.78$, $SD = 12.38$) ($t(137) = -1.117$, ns). Internalizing behavior scores did significantly differ between males ($M = 45.69$, $SD = 11.67$) and females ($M = 52.10$, $SD = 14.21$) ($t(137) = -2.894$, $p = .004$), with females exhibiting significantly more internalizing behaviors than males. A univariate ANOVA was conducted to evaluate whether externalizing and internalizing behaviors differed across racial/ethnic groups (grouped as Hispanic/Latinx, Black, White, and Other). The results indicated there were no significant differences in externalizing behaviors ($F(135) = .688$, ns) and internalizing behaviors ($F(135) = .075$, ns) across racial/ethnic groups.

Additionally, a paired samples t-test was conducted to evaluate whether externalizing and internalizing behaviors changed across time for participants. Externalizing behavior scores did significantly decrease from Time 1 ($M = 49.80$, $SD = 9.44$) to Time 2 ($M = 44.68$, $SD = 11.94$) ($t(137) = 6.640$, $p < .001$). Furthermore, internalizing behavior scores did significantly decrease from Time 1 ($M = 57.28$, $SD = 10.98$) to Time 2 ($M = 48.90$, $SD = 13.38$) ($t(137) = 8.530$, $p < .001$).

Well-Being

Externalizing Behaviors

Results from the examination of the association between well-being with household dysfunction and externalizing behaviors indicated no significant main effect of household dysfunction on externalizing behaviors. Additionally, the main effect of well-being on externalizing behaviors was not significant. Finally, the interaction between household dysfunction and well-being was not significant.

Internalizing Behaviors

The examination of the association between well-being with household dysfunction and internalizing behaviors indicated no significant main effect of household dysfunction on internalizing behaviors. Additionally, the main effect of well-being on internalizing behaviors was not significant. Finally, the interaction between household dysfunction and well-being was not significant.

Family Connectedness

Externalizing Behaviors

Results from the examination of the association between family connectedness with household dysfunction and externalizing behaviors indicated adolescents who had higher levels of family connectedness exhibited fewer externalizing behaviors than their counterparts who possessed lower levels of family connectedness. The main effect of household dysfunction on externalizing behaviors was not significant. The interaction between household dysfunction and family connectedness was statistically significant. All regression coefficients are presented in Table 3.

This interaction between household dysfunction and family connectedness was probed by examining Johnson-Neyman significance regions in SPSS PROCESS (see supplemental table S1). Results indicated that household dysfunction was associated with greater externalizing behaviors only at extremely low levels of family connectedness (approximately 2 SD below M). However, at higher levels of family connectedness, the association between household dysfunction and externalizing behaviors was no longer significant. See Figure 1 for a visual of the simple slopes and the corresponding statistics.

Internalizing Behaviors

Results from the examination of the association between family connectedness with household dysfunction and internalizing behaviors indicated no significant main effect of household dysfunction on internalizing behaviors. Additionally, the main effect of family connectedness on internalizing behaviors was not significant. Finally, the interaction between household dysfunction and family connectedness was not significant.

Peer Connectedness

Externalizing Behaviors

Results from the examination of the association between peer connectedness with household dysfunction and externalizing behaviors indicated no significant main effect of household dysfunction on externalizing behaviors. However, the main effect of peer connectedness on externalizing behaviors was significant, with higher levels of peer connectedness

being associated with greater externalizing behaviors. Finally, the interaction between household dysfunction and peer connectedness was not significant.

Internalizing Behaviors

Results from the examination of the association between peer connectedness with household dysfunction and internalizing behaviors indicated no significant main effect of household dysfunction on internalizing behaviors. Additionally, the main effect of peer connectedness on internalizing behaviors was not significant. Finally, the interaction between household dysfunction and peer connectedness was not significant.

Discussion

Dysfunction within the household environment can exacerbate the development of externalizing and internalizing behaviors during adolescence (Björkenstam et al., 2016; Sacks & Murphey, 2018). However, individual and social protective factors, such as adolescents' well-being and family and peer connectedness, have the potential to buffer against these behavioral effects (Shapiro & Steinberg, 2013). The results revealed that the association between household dysfunction and externalizing behaviors was not significant among adolescents with higher levels of family connectedness. This observed protective effect of family connectedness on externalizing behaviors aligns with previous literature indicating that high levels of family connectedness are associated with fewer maladaptive behaviors (Foster et al., 2017; Willems et al., 2020). Furthermore, past research has suggested that at-risk adolescents possessing better connections with their parents show fewer conduct issues (Foster et al., 2017). This positive behavioral impact may be a result of connections with others, especially parents, leading to a sense of belonging, improved communication, and belief in oneself (Foster et al., 2017). It is noted that even though family connectedness and household dysfunction are inherently related, the only significant correlation between family connectedness and an aspect of household dysfunction was marginal, reducing concerns about the collinearity of the two variables.

One reason family connectedness may be protective is that being connected and involved with one's family has been shown to increase coping skills and decrease mental distress when experiencing mental health issues (Boritz et al., 2021). Another mechanism by which family connectedness may minimize maladaptive behaviors is self-control, which is implicated in the expression of externalizing behaviors (Gottfredson & Hirschi, 1990). Findings from prior studies have shown that family connectedness cultivates the development of behavioral self-control, such that adolescents with higher levels of family connectedness exhibit better impulse control (Willems et al., 2020). Nevertheless, it is important to acknowledge that this finding was likely driven by a small subset of the sample who showed low levels of family connectedness.

Therefore, it is important for future research to replicate this finding.

It is possible that family connectedness did not impact internalizing behaviors due to the potential inheritability of depressive symptoms (Hanington et al., 2010). Thus, adolescents may have already exhibited internalizing behaviors, including being withdrawn from other people, and connections with others would possibly not have an impact on their behaviors. Future research should look at the role of parental depression to account for the potential inheritance of depression. Additionally, there was a significant correlation between family connectedness and internalizing behaviors at Time 1, suggesting that this association is concurrent rather than longitudinal.

In addition, peer connectedness was not found to be a protective factor for externalizing and internalizing behaviors. Rather, the results indicated that higher levels of peer connectedness were associated with greater externalizing behaviors. This finding may have been due to the possible confound of peer norms. Prior research has indicated that adolescents oftentimes choose friends with similar levels of maladaptive behaviors (Franken et al., 2016), suggesting that adolescents with varying levels of externalizing behaviors have friends with similar behaviors. Thus, adolescents' connections with their peers would not be protective against externalizing behaviors, due to the established norms of their peer group. The confounding effect of peer norms may also explain why there was no association between peer connectedness and internalizing behaviors.

An unexpected finding in this study was that household dysfunction did not have a significant effect on adolescents' future externalizing and internalizing behaviors. Past research suggests that adverse childhood experiences, including dysfunction within the household, impact future psychopathology (Björkenstam et al., 2016; Sacks & Murphey, 2018). However, this finding may be due to the household dysfunction study variables not capturing the full nature of household dysfunction. Previous literature on ACEs and household dysfunction has included variables of violence against the mother-figure (Felitti et al., 2019), a factor that was not measured in the current study. It is possible that due to this limitation, the household dysfunction variable explored in the current study was missing a significant aspect of household dysfunction.

Additionally, this finding may have been due to the study's timespan of one year being too short to examine the behavioral effects of household dysfunction. Prior research has suggested that adverse childhood experiences, including household dysfunction, have long-term consequences on individuals' well-being and functioning during adulthood (Anda et al., 2004). Therefore, extending the length of the study to late adolescence or adulthood may have resulted in an impact of adolescents' household dysfunction on their behavioral development. Furthermore, this study only looked at the effects of household dysfunction among middle school-aged children, rather than older adolescents. Current literature suggests that

adverse experiences, such as household dysfunction, impact children and adolescents differently (Turner et al., 2020); however, less is known about the effects of household dysfunction across adolescence. It is possible that, as adolescents age and gain more independence from their parents, their emotional and behavioral response to household dysfunction changes or becomes more apparent.

Additionally, personal well-being was not found to have a significant impact on the development of externalizing and internalizing behaviors. This finding may be due to the contrasting nature of well-being as a form of resilience after adverse occurrences. In some instances, experiencing adversity during childhood is associated with lower resilience, and in others adversity provides the opportunity for individuals to develop coping mechanisms and resilience-focused skills (Harms et al., 2018). In essence, adversity can either be the reason one develops resilience or why they do not overcome difficulties. As such, it is possible that participants in the current study did not develop individual resilience-skills and their well-being was not a strong enough protective factor. In addition, the well-being variable did not fully capture the range of the 7 C's of resilience defined in the positive youth development literature (Ginsburg, 2020). Although personal well-being has a positive impact on behavioral development (Hoyt et al., 2012), well-being has not been identified as a part of the 7 C's of resilience in prior research.

Strengths and Limitations

There are several limitations of this study that are important to consider when interpreting the results. One limitation was that, overall, parents endorsed relatively low levels of household dysfunction, as indicated by scores on parental depression, incarceration, substance use, and marital status. This low endorsement of household dysfunction among participants likely biased the results for the association between household dysfunction and adolescents' psychological outcomes. Furthermore, the low rates of household dysfunction suggest the sample used in this study is not representative of the broader population. National epidemiological reports on childhood adversity have indicated that 20.1% of children experienced divorce or parental separation, 10.7% experienced household substance use, 8.6% experienced household mental illness, and 6.9% had an incarcerated parent (Child and Adolescent Health Measurement Initiative, 2013). As such, future research should replicate the current study using larger, more nationally representative samples.

An additional limitation in this study was that the household dysfunction variables were only explored in the participants' parents who attended the study session with them. It is possible that other adults in the household, or even other members such as siblings, may have contributed to household dysfunction, yet were not explored in this study. Additionally, the parent incarceration variable only explored whether the parent had ever been incarcerated, not whether they had been

incarcerated recently or during their child's lifetime. It is important to consider the timing of parents' incarceration, since parents who were incarcerated before having their child may have had less of a contribution to household dysfunction than if they were recently incarcerated.

Another limitation in this study was that it was only one year long due to the practical constraints of administering questionnaires. Future research should replicate the current study longitudinally across additional, larger time points. Additionally, this study only explored the study variables among adolescents aged 11-15 years old, due to the constraints of using data from a larger study. It would be useful to study the same research questions among adolescents of older ages in the future to compare how the effects of household dysfunction and resilience factors might change in older populations.

Despite these limitations, a strength of the study was the exploration of both individual (well-being) and environmental (family and peer connectedness) resilience variables. This variety of resilience variables allowed for the investigation of protective factors occurring in multiple domains of adolescents' lives. Additionally, participants were diverse in terms of gender identity and racial/ethnic backgrounds, allowing the current study to capture the experiences of adolescents from diverse backgrounds. Finally, the examination of adolescents' externalizing and internalizing symptoms across two time points provided greater confidence in the directionality of the associations between family connectedness and adolescent psychopathology.

Conclusions

Overall, results from this study suggest that household dysfunction is a risk factor for future externalizing behaviors among adolescents with extremely low levels of family connectedness. However, high family connectedness may serve as a protective factor against the development of externalizing behaviors. This effect is not seen to be true for adolescents' internalizing behaviors. Surprisingly, peer connectedness and personal well-being were not found to be as protective in nature as indicated in previous literature, suggesting that intervention and prevention methods for externalizing behaviors that focus on improving relationships within the family may be most successful. Despite adolescence being a period when youth oftentimes rely more on their peers for support (Nickerson & Nagle, 2005), these results suggest that parents and family members are still influential for behavioral development, possibly more than that of adolescents' peers. As such, parents and family members should strive to foster connectedness with adolescents in order to decrease the development of externalizing behaviors. All in all, family connectedness is an important influence on adolescent behaviors; however, dysfunction within the home and its behavioral effects are complex, clearly revealing a need for future research in this domain.

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Appendix

Table 1

Descriptive statistics for primary study variables.

Descriptives	Min	Max	M	SD
T1 Externalizing Behaviors	34	72	49.95	9.245
T2 Externalizing Behaviors	29	91	44.69	11.901
T1 Internalizing Behaviors	33	78	56.67	11.398
T2 Internalizing Behaviors	27	90	49.01	13.392
Parent Depression	0	24	3.766	4.172
Parent Substance Use	0	5.67	.806	1.007
T2 Well-being	1	6	4.444	1.26
T1 Family Connectedness	2	5	4.279	.699
T1 Peer Connectedness	2.33	5	4.046	.712

Note. Parent depression and parent substance use are parent-reported, whereas every other measure is teen-reported.

Table 2

Correlations among primary study variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. T1 Externalizing	---	.663**	.524**	.374**	-.247**	-.134	-.236**	.095	.063	-.027	.262**	.143	-.084	-.042	-.031	-.089
2. T2 Externalizing		---	.402**	.682**	-.065	.071	-.242*	-.042	.03	.132	.198*	.087	-.107	.024	-.022	-.095
3. T1 Internalizing			---	.566**	-.171*	-.084	-.177*	.05	.069	.042	.237**	.057	-.062	.033	-.047	-.232**
4. T2 Internalizing				---	-.071	.033	-.172	-.13	.022	.106	.177	.01	.002	.017	-.04	-.240**
5. T1 Family Connect.					---	.419**	.340**	-.077	-.257**	-.04	-.039	-.066	.075	-.035	.046	-.003
6. T1 Peer Connect.						---	.091	-.173*	-.074	.023	.085	.07	-.021	.028	-.109	-.095
7. Well-being							---	.011	.034	.026	.05	-.042	.003	-.055	.139	.176*
8. Parent Depression								---	.042	.116	.197*	.077	-.075	-.019	.017	-.111
9. Parent Marital Status									---	.224**	.09	-.272**	.339**	.017	-.082	-.138
10. Parent Incarceration										---	.279**	-.01	.239**	-.143	.033	-.045
11. Parent Substance Use											---	.229**	.063	-.238**	-.057	-.095
12. White												---	-.362**	-.478**	-.242**	.092
13. Black													---	-.401**	-.203**	-.015
14. Hispanic/Latinx														---	-.268**	-.051
15. Other															---	-.036
16. Male																---

Note. Parent depression, marital status, incarceration, and substance use are parent-reported, whereas every other measure is teen-reported; connect = connectedness.

* $p < .05$; ** $p < .01$; *** $p < .001$

Table 3

Regression Analysis for Household Dysfunction Predicting Externalizing Behaviors (Family Connectedness)

Step	Variable	B	SE (B)	Std. b	R^2
1	T1 Externalizing	.882	.087	.702	.496
	Male	-1.938	1.633	-.082	
	Black	.101	2.301	.003	
	Hispanic	2.441	2.036	.096	
	Other	-1.330	2.581	-.040	
2	Household Dysfunction	.207	.966	.015	.491
3	Family Connectedness	1.572	1.25	.09	.494
4	Dysfunction x Family Connectedness	-2.951*	1.449	-.909	.509

Note. Time 1 externalizing behaviors, gender and race/ethnicity are control variables. "White" was omitted as the race/ethnicity reference group. Household dysfunction is parent-reported. Dysfunction x Family Connectedness is the interaction between household dysfunction and family connectedness. * $p < .05$; ** $p < .01$; *** $p < .001$

Table 4

Regression Analysis for Household Dysfunction Predicting Internalizing Behaviors (Family Connectedness)

Step	Variable	B	SE (B)	Std. <i>b</i>	<i>R</i> ²
1	T1 Internalizing	.67	.093	.58	.367
	Male	-2.928	2.049	-.115	
	Black	2.28	2.76	.073	
	Hispanic	1.494	2.448	.055	
	Other	-1.079	3.125	-.030	
2	Household Dysfunction	-.908	1.18	-.062	.365
3	Family Connectedness	.792	1.508	.042	.36
4	Dysfunction x Family Connectedness	-1.441	1.771	-.412	.358

Note. Time 1 internalizing behaviors, gender and race/ethnicity are control variables. "White" was omitted as the race/ethnicity reference group. Household dysfunction is parent-reported. Dysfunction x Family Connectedness is the interaction between household dysfunction and family connectedness.

Table 5

Regression Analysis for Household Dysfunction Predicting Externalizing Behaviors (Peer Connectedness)

Step	Variable	B	SE (B)	Std. <i>b</i>	<i>R</i> ²
1	T1 Externalizing	.882	.087	.702	.496
	Male	-1.938	1.633	-.082	
	Black	.101	2.301	.003	
	Hispanic	2.441	2.036	.096	
	Other	-1.330	2.581	-.040	
2	Household Dysfunction	.207	.966	.015	.491
3	Peer Connectedness	2.915*	1.181	.176	.515
4	Dysfunction x Peer Connectedness	-1.320	1.359	-.401	.515

Note. Time 1 externalizing behaviors, gender and race/ethnicity are control variables. "White" was omitted as the race/ethnicity reference group. Household dysfunction is parent-reported. Dysfunction x Peer Connectedness is the interaction between household dysfunction and peer connectedness. * $p < .05$; ** $p < .01$; *** $p < .001$

Table 6

Regression Analysis for Household Dysfunction Predicting Internalizing Behaviors (Peer Connectedness)

Step	Variable	B	SE (B)	Std. <i>b</i>	<i>R</i> ²
1	T1 Internalizing	.67	.093	.58	.367
	Male	-2.928	2.049	-.115	
	Black	2.28	2.76	.073	
	Hispanic	1.494	2.448	.055	
	Other	-1.079	3.125	-.030	
2	Household Dysfunction	-.908	1.18	-.062	.365
3	Peer Connectedness	.66	1.439	.037	.36
4	Dysfunction x Peer Connectedness	1.434	1.681	.405	.358

Note. Time 1 internalizing behaviors, gender and race/ethnicity are control variables. "White" was omitted as the race/ethnicity reference group. Household dysfunction is parent-reported. Dysfunction x Peer Connectedness is the interaction between household dysfunction and peer connectedness.

Table 7

Regression Analysis for Household Dysfunction Predicting Externalizing Behaviors (Well-being)

Step	Variable	B	SE (B)	Std. <i>b</i>	<i>R</i> ²
1	T1 Externalizing	.929	.102	.72	.513
	Male	-2.221	1.933	-.089	
	Black	.596	2.638	.02	
	Hispanic	2.228	2.432	.082	
	Other	-2.341	3.127	-.064	
2	Household Dysfunction	.38	1.221	.026	.508
3	Well-being	-1.195	.835	-.119	.514
4	Dysfunction x Well-being	-1.4	.963	-.468	.521

Note. Time 1 externalizing behaviors, gender and race/ethnicity are control variables. "White" was omitted as the race/ethnicity reference group. Household dysfunction is parent-reported. Dysfunction x Well-being is the interaction between household dysfunction and adolescent well-being.

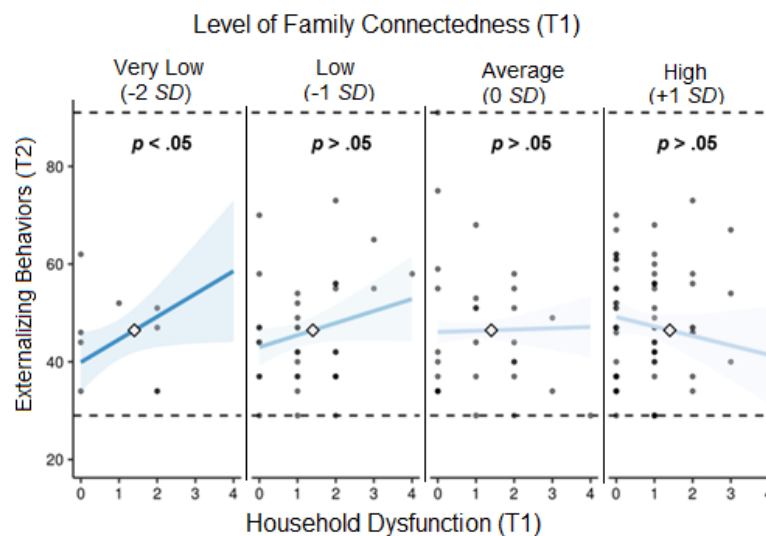
Table 8

Regression Analysis for Household Dysfunction Predicting Internalizing Behaviors (Well-being)

Step	Variable	B	SE (B)	Std. <i>b</i>	<i>R</i> ²
1	T1 Internalizing	.774	0.1	.653	.473
	Male	-3.591	2.237	-.135	
	Black	2.12	2.904	.067	
	Hispanic	1.605	2.694	.055	
	Other	-1.696	3.488	-.043	
2	Household Dysfunction	-.105	1.369	-.007	.466
3	Well-being	-1.072	0.908	-.100	.469
4	Dysfunction x Well-being	6.242	5.139	.394	.473

Note. Time 1 internalizing behaviors, gender and race/ethnicity are control variables. "White" was omitted as the race/ethnicity reference group. Household dysfunction is parent-reported. Dysfunction x Well-being is the interaction between household dysfunction and adolescent well-being.

Figure 1



The figure is composed of four graphs, each for a level of adolescent-reported family connectedness: one and two standard deviations below the mean, at the mean, and one standard deviation above the mean. A graph for family connectedness at two standard deviations above the mean was excluded as it possessed zero data points. Household dysfunction, which was composed of parent-reported variables of parent mental illness, marital status, substance use, and incarceration, ranged from low to high. Externalizing behaviors, self-reported by adolescent participants, ranged from low to high. For the graph with adolescents possessing family connectedness two standard deviations below the mean level, as household dysfunction increased adolescent externalizing behaviors increased as well. The other levels of family connectedness did not show a significant association between household dysfunction and externalizing behaviors.

Supplemental Material

Table S1

Conditional effect of household dysfunction at values of the family connectedness

Values of Family Connectedness (T1)	B	SE (B)	<i>t</i>	<i>p</i>	95% Confidence Interval	
					Lower Bound	Upper Bound
2.667	4.914	2.424	2.027	0.045	0.104	9.724
2.783	4.569	2.270	2.013	0.047	0.066	9.073
2.900	4.225	2.118	1.995	0.049	0.023	8.427
2.958	4.055	2.044	1.984	0.050	0.000	8.111
3.017	3.881	1.969	1.971	0.052	-0.025	7.787
3.133	3.537	1.823	1.940	0.055	-0.080	7.153
3.250	3.192	1.681	1.899	0.061	-0.144	6.528
3.367	2.848	1.546	1.843	0.068	-0.218	5.914
3.483	2.504	1.417	1.767	0.080	-0.307	5.314
3.600	2.159	1.297	1.665	0.099	-0.414	4.733
3.717	1.815	1.190	1.526	0.130	-0.545	4.175
3.833	1.471	1.098	1.340	0.183	-0.707	3.649
3.950	1.126	1.026	1.098	0.275	-0.909	3.161
4.067	0.782	0.978	0.800	0.426	-1.158	2.722
4.183	0.438	0.958	0.457	0.649	-1.462	2.338
4.300	0.094	0.967	0.097	0.923	-1.826	2.013
4.417	-0.251	1.006	-0.249	0.804	-2.246	1.744
4.533	-0.595	1.070	-0.556	0.579	-2.717	1.527
4.650	-0.939	1.155	-0.813	0.418	-3.231	1.352
4.767	-1.284	1.257	-1.021	0.310	-3.778	1.211
4.883	-1.628	1.373	-1.186	0.239	-4.352	1.096
5.000	-1.972	1.499	-1.316	0.191	-4.946	1.001

Note. Results obtained using Johnson-Neyman regions of significance output from SPSS PROCESS Version 3.4 (Hayes, 2019)

Sydney H. White, BA

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Sydney H. White graduated with departmental honors from Johns Hopkins University with a Bachelor of Arts in Psychology and a minor in Spanish for the Professions in December 2021. As an undergraduate, Sydney was a research assistant in Dr. Fernando Goes' lab at the Johns Hopkins Mood Disorders Center, studying Ketamine versus Electroconvulsive Therapy (ECT) as treatments for Major Depressive Disorder. During the summer of 2021, Sydney was selected to participate in a National Science Foundation Research Experience for Undergraduates, through which she completed her research and paper. While at Johns Hopkins, she spent much of her time working to improve mental health and equal access to adequate health care in the Baltimore community, primarily through her work interpreting at vaccine sites and translating food stamp applications for the Hispanic population of Maryland. She currently works as a research coordinator under Dr. Roland Griffiths at the Johns Hopkins Center for Consciousness and Psychedelics Research, primarily on the Anorexia Nervosa study. After working in a post-baccalaureate position, she hopes to pursue her Ph.D. in Clinical Psychology.



Was there a particular experience that sparked your research interests?

An experience that sparked my research interests was my work at the Johns Hopkins Mood Disorders Center! This was my first glimpse into the realm of clinical research, as I worked on a study comparing the use of electroconvulsive therapy (ECT) and intravenous ketamine for treatment-resistant depression. Shadowing ketamine infusions showed me how life-changing research can be for individuals who, previously, had lost hope for potential treatments, and from then on, I knew I wanted to pursue groundbreaking research!

Who has been the most influential person in your life?

The most influential people in my life (aside from my parents, of course) have been the female professors I got to know in my time at JHU. Seeing such amazing female scientists breaking down gender barriers gave me someone to look up to and someone to identify with, as I pursued my degree. Two, in particular, Dr. Allison Papadakis and Dr. Chelsea Howe, introduced me to the world of clinical

psychology, and their mentorship has been an integral part of my educational experience.

What is your greatest accomplishment?

My greatest accomplishment thus far has for sure been walking across the stage at commencement to receive my degree. After spending countless hours studying, researching, volunteering, and so much more, it meant the world to finally shake the hand of our school's president and solidify the end of my undergraduate career. It was a moment in which I truly felt proud of myself, and to have my extended family there meant the world. It wasn't an easy four years, but we all were able to push through and succeed.

Where do you see yourself in 10 years?

In 10 years, I hope to be doing research and teaching at a university in the United States, specifically in the abnormal psychology and clinical treatment space. I also see myself continuing my work in the realm of psychedelic treatment, with hopes of finding solutions to a range of treatment-resistant disorders.

The Moderating Effect of Comorbidity and Mediating Effect of Hair Cortisol on the Relationship Between Trauma and PTSD in the United States Veteran Population

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Post-traumatic stress disorder (PTSD) is a mental health disorder characterized by high stress, hyperarousal, depressed mood, and avoidant/intrusion symptoms occurring after exposure to acute or prolonged trauma. PTSD is often comorbid with other disorders, and in the case of comorbidity, patients have a worse prognosis. Studying the risk factors and indicators of these disorders can help clinicians prevent and treat PTSD, including PTSD with comorbidities such as major depressive disorder (MDD) and alcohol use disorder (AUD). Biomarkers are an efficient and objective way to study PTSD. A common biomarker of stress being cortisol: an adrenal hormone and the end-product of the hypothalamic-pituitary-adrenal (HPA) axis in humans. This study explores the mediating effect of hair cortisol levels on the relationship between trauma exposure and PTSD, moderated by both MDD and AUD comorbidities in the veteran population. We hypothesized that those with increased trauma exposure would also have increased cortisol levels, which in turn would be associated with more severe PTSD. Furthermore, we hypothesized that the presence of a comorbidity would increase the strength of the positive relationship between trauma exposure and hair cortisol levels. The results showed that the mediating effect of hair cortisol was not significant, yet the moderating effect of depressive symptoms was. We conclude that the strength of the trauma-to-PTSD model could be moderated by symptoms of depression, rather than mediated by cortisol levels.

Keywords: PTSD, Cortisol, Hypothalamic-Pituitary-Adrenal axis, Comorbidity, MDD, AUD.

Post-traumatic stress disorder (PTSD) is defined as a chronic psychological disorder that can develop after exposure to a traumatic event, with intrusive and avoidant symptoms such as flashbacks, nightmares, and severe anxiety (Lancaster et al., 2016). Trauma itself is an event that causes high levels of fear, stress, or shock, and is often characterized by apparent harm or danger. PTSD can occur alone, but it also commonly occurs alongside other mental health disorders. It has been reported that approximately 80% of patients with PTSD have at least one comorbid psychiatric disorder (Grinage, 2003). Epidemiological studies show an overall increased risk for a wide range of comorbid mental health disorders for those with PTSD such as major depressive disorder (MDD), generalized anxiety disorder (GAD), panic disorder, conduct disorder (CD), substance use disorder (SUD), and more (Scherrer et al., 2008). The most common disorders diagnosed in conjunction with PTSD include depressive disorder, substance use disorders, and anxiety disorders (Brady et al., 2000). Additionally, data collected in 2007 by Harvard's National Comorbidity Survey indicate a lifetime prevalence of 6.8% for PTSD (Alegria et al., 2016), while an earlier National Comorbidity Survey found that the

prevalence of at least one lifetime traumatic event was around 60.7% for men and 51.2% for women (Kessler et al., 1995). Although not all who are exposed to trauma develop PTSD, exposure to trauma is both a risk factor and diagnostic criteria for the disorder. Thus, there may be other factors affecting this relationship between trauma and PTSD outcomes, comorbidities being one of them.

Comorbidity

The American Psychological Association (APA) defines psychological comorbidity as the simultaneous presence in an individual of more than one illness, disease, or disorder (APA Dictionary of Psychology, n.d.). In the case of the current study, comorbidity is defined as having both PTSD and another disorder, specifically MDD or AUD. MDD is one of the most prevalent disorders within the U.S. veteran community, at around 13.5%. Additionally, substance use disorders are nearly as common as PTSD, with a prevalence of 8.3% (Trivedi et al., 2015). The literature has shown that the co-occurrence of PTSD with either MDD or AUD is significantly high, indicating that there are etiological similarities between the disorders. One meta-analysis

conducted in 2013 reviewed over 57 studies and found that 52% of service members met diagnostic criteria for both PTSD and MDD (Rytwinski et al., 2013). Another study from 2014 found that the rate of comorbidity between PTSD and AUD could range anywhere from 30 to 59% (Raleyski, et al., 2014). Co-occurrence of these disorders can make it harder to individually treat patients, and it often worsens their prognosis as well. A worse prognosis can mean worse psychiatric outcomes, more complex treatment/management, and an increase in the cost of treatment (Valderas et al., 2009). Thus, studying the causes and mechanisms by which these disorders occur can be an important step in helping prevent and treat these highly co-occurring mental health disorders.

Cortisol

As no objective laboratory-based diagnostic test for PTSD currently exists, considerable effort has been spent on the pursuit of such biomarkers, which could help clinicians assess and treat patients more rapidly and efficiently (Dean et al., 2020). One common biomarker of stress is cortisol, an adrenal hormone and the end product of the hypothalamic-pituitary-adrenal (HPA) axis in humans. The HPA axis is the major neuroendocrine stress-response system (Chen et al., 2016), a main function of the HPA axis being the secretion of cortisol. Cortisol inhibits the stress response in an attempt to return the body to homeostasis (Chen et al., 2016), working in a self-regulating, allostatic manner to return our bodily systems to our “set point”, our body’s baseline level. (Stephens & Wand, 2012). However, if the body is overstimulated and in a constant state of high pressure, the HPA axis could become overworked, resulting in downregulation of cortisol production (Pan et al., 2018). Long-term activation of the HPA axis (such as in high states of alertness in PTSD patients) can lead to various negative outcomes, such as chronic basal hypersecretion, sensitized stress responses, and adrenal exhaustion (Herman et al., 2016). Moreover, if the HPA axis is not restored to normal, then abnormal cortisol levels may arise in patients with PTSD.

Evidence in the literature shows the important role of dysfunctional cortisol secretion in PTSD, and how it is related to the development, maintenance, and treatment of the disorder (Hummel et al., 2021). Hummel et al. (2021) emphasizes the use of hair cortisol analysis as an assessment of secretion over longer periods of time, for up to several months. Thus, cortisol could be used as a biomarker for patients with PTSD (Pan et al., 2018). Interestingly, Patients with PTSD had lower cortisol levels and lower cortisol stress reactivity than those with MDD (Petrowski et al., 2020). Research has shown that the relationship between the HPA axis and the brain’s reward system is associated with alcohol dependence and use. However, this relationship between the HPA axis, reward, and alcohol is complex as it depends on the stage of the substance use disorder (Stephens & Wand, 2012). Thus, the literature offers some insight into the differences in cortisol levels based on different disorders, and raises the question of whether cortisol

functions as a successful biomarker for PTSD alone or in combination with other disorders.

Hair Cortisol

As a biomarker, cortisol is found in many parts of the body, such as hair, blood, saliva, and urine. However, these amounts of cortisol only provide a reflection of short-term hormone levels, therefore being an indication of only acutely circulating cortisol production (Pan et al., 2018). Alternatively, hair cortisol serves as a valid and reliable measure of long-term cortisol secretion (Stalder, 2012). Not only is the extraction of hair less invasive than a blood test, it is also easily stored and can be kept at room temperature, which provides great utility for researchers (Pan et al., 2018). In sum, given the reliability and validity of hair cortisol in a research setting, and the high prevalence of disorders such as PTSD, MDD, and AUD in the military (Xue et al., 2015), this study will investigate hair cortisol as a biomarker in relation to the U.S. veteran population.

Veteran Etiology

Several factors put military service members at a higher risk for experiencing trauma than other citizens, meaning many veterans suffer from PTSD later in life. As previously stated, trauma is an event that causes high levels of fear, stress, or shock. Service members are often exposed to life threatening situations, whether directly or indirectly. Although there are further risk factors beyond just entering the military that increase risk for developing PTSD, as not all who are exposed to trauma will develop the disorder, there is indication that there are etiological differences that can increase its risk for development (Xue et al., 2015). According to Fontana and Rosenheck (1993), active service members who were younger when they entered the military and/or who joined the military willingly experienced more severe PTSD symptoms than older or conscripted service members, respectively. Additionally, they found that higher levels of combat exposure, witnessing abusive violence, and receiving disciplinary action all led to worse PTSD symptoms. Other studies have shown that the intensity of trauma is a strong predictor of PTSD outcomes, as well as lack of social support, major life stressors, and adverse childhood events (Xue et al., 2015). Xue et al. also found that in the veteran population, prevalence of combat-related PTSD ranged anywhere from 1.09% to 34.84%. The risk of experiencing traumatic events in the military is constant over the course of active service, and thus, this population could benefit from further investigation into the associations between PTSD severity and other factors. In this case, that means comorbidity, hair cortisol, and trauma exposure.

Current Study

One meta-analysis on the relationship between hair cortisol and MDD reported higher cortisol levels in patients’ first

depressive episode compared to recurrent MDD and controls, as well as finding that patients with comorbid MDD and anxiety disorder had higher cortisol than controls (Psarraki et al., 2021). However, another study within the meta-analysis found no significant difference between the hair cortisol of depressed patients and healthy controls. They clarified that this contradiction among results shows that there is room for improvement in this research field (Psarraki et al., 2021), of which we hope to contribute. Additionally, a 2016 study on the levels of hair cortisol in relation to alcohol misuse revealed that those with higher hair cortisol levels show increased sedation after drinking alcohol, which in turn puts them at a higher risk for AUD due to the desirability of alcohol's calming ability (Szabo et al., 2020; Brkic et al., 2016). These studies informed our decision to investigate the effects of PTSD comorbid with MDD and AUD on hair cortisol levels. Considering the state of our knowledge and the importance of clarifying the role of cortisol as a PTSD biomarker, we hypothesized that trauma exposure would lead to increased cortisol levels, which in turn would increase risk for PTSD comorbid with both MDD and alcohol use disorder (AUD). Furthermore, we hypothesized that the presence of a psychiatric comorbidity (in this case, MDD or AUD) would increase the strength of the positive relationship between trauma exposure and hair cortisol levels; i.e., if patients had a pre-existing mental health condition. We expected they would have an increased stress response, and in turn, higher cortisol levels.

Methods

Participants

This analysis utilized data collected in the "Genetic Biomarkers of PTSD and Chronic Stress in Veterans" study undertaken at SUNY Oswego, SUNY Upstate, & Syracuse University. The current study was designed to evaluate cortisol as a mediator of the relationship between trauma and PTSD outcomes, moderated by psychiatric comorbidity in veterans from the United States Armed Forces. Psychological assessment data was collected via a Qualtrics survey sent to the participants. In total, 53 subjects participated in the study, of whom 35 completed all the questionnaires and submitted hair samples. Thus, 18 of the participants were excluded from analyses due to not completing all the questionnaires, or for failing to submit their hair sample.

Table 1

Demographics of Sample

	Male (N=41)	Female (N=12)	Overall (N=53)
Age			
Mean (SD)	45.9 (10.9)	42.5 (8.30)	45.1 (10.4)
Median [Min, Max]	46.0 [30.0, 69.0]	42.0 [30.0, 53.0]	45.0 [30.0, 69.0]
Ethnicity			
Do Not Wish to Answer	0 (0%)	0 (0%)	0 (0%)
Hispanic or Latino	5 (12.2%)	1 (8.3%)	6 (11.3%)
Not Hispanic or Latino	36 (87.8%)	11 (91.7%)	47 (88.7%)
Race			
Do Not Wish to Answer	2 (4.9%)	0 (0%)	2 (3.8%)
American Indian or Alaskan native	2 (4.9%)	0 (0%)	2 (3.8%)
Asian	0 (0%)	1 (8.3%)	1 (1.9%)
Black or African American	2 (4.9%)	3 (25.0%)	5 (9.4%)
Native Hawaiian or other Pacific Islander	0 (0%)	1 (8.3%)	1 (1.9%)
White	34 (82.9%)	7 (58.3%)	41 (77.4%)
Other	1 (2.4%)	0 (0%)	1 (1.9%)

Procedure

Participants who signed up for the study received both an online survey link and a hair extraction kit. Once participants completed the surveys and submitted their hair sample, they were compensated with a money order of \$50 sent in the mail. All participants provided informed consent before partaking in the study in accordance with APA ethical standards of the Syracuse University IRB.

Measures

All the measures used in the study were selected based on their wide utilization in PTSD research and were self-administered through Qualtrics.

Posttraumatic Stress Disorder Checklist (PCL-5)

The Posttraumatic Stress Disorder Checklist (PCL-5) is a 20-item self-report measure assessing the symptoms of PTSD according to DSM-5 criteria. It is used to not only monitor PTSD symptoms, but also to screen individuals and make provisional diagnoses. In this case, it was used to measure our outcome variable of PTSD symptom severity. The PCL-5 is scored based on a Likert scale ranging from 0-4, with 0 meaning *not at all*, 2 meaning *moderately*, and 4 meaning *extremely*. One example question is: "how much have you been bothered by repeated, disturbing, and unwanted memories of the stressful experience" (Blevins et al., 2015). The total symptom severity score ranges from 0-80, with 0 being mild and 80 being severe. A total score can be obtained by summing the scores across all items. Additionally, cluster severity scores are calculated by summing the scores for the items within a given cluster: intrusion symptoms are items 1-5, avoidance symptoms are items 6 and 7, negative alterations in cognition and

mood are items 8- 14, and alterations in mood/reactivity are measured by items 15-20 (Blevins et al., 2015).

Combat Exposure Scale (CES)

The Combat Exposure Scale (CES) is a measure of trauma exposure, which in this case, is our predictor variable. The CES was created as a measure of the subjective reports of wartime stressors experienced by active-duty service members (Keane et al., 1989). Each item of the CES is scored on a scale of 0 or 1, with 0 being *No* and 1 being *Yes*. For example, one question is: "I personally witnessed someone from my unit, or an ally unit, being seriously wounded or killed" (Keane et al., 1989). The CES has been widely used in the literature, and results show it is both a reliable and valid measure of trauma exposure. In terms of its reliability, one study showed strong internal consistency ($\alpha = 0.85$), indicating that the items are measuring the construct (Keane et al., 1989). Additionally, test-retest reliability was measured by giving the scale to 39 Vietnam-theater veterans twice with a week in between, and the results found a correlation of $r(29) = .97, p < .0001$, an indication of excellent test-retest reliability (Keane et al., 1989).

Beck Depression Inventory II (BDI-II)

The Beck Depression Inventory (BDI-II) is a self-report measure assessing the symptoms of MDD according to DSM-5 criteria, and it was employed as the measure for one of the moderators in our model. It is one of the most widely recognized and employed instruments for measuring the severity of self-reported depression in a wide range of age groups, and both its validity and reliability have been established across many clinical populations (Beck et al., 1988). One study performed in Germany tested several types of reliability for the BDI-II, finding in all cases significant reliability (Kühner et al., 2007). Test-retest reliability was significant with $r = 0.78, (p < 0.001)$. Additionally, these investigators found an internal consistency of $\alpha = 0.84$, indicating high internal consistency (Kühner et al., 2007). The items of the BDI-II are scored based on a Likert scale ranging from 0-3, with 0 being minimal manifestation of the symptom, and 3 being extreme manifestation of the symptom. One example of an item on the assessment is: "I feel my future is hopeless and will only get worse" (Beck et al., 1988), with answers ranging from 0 = *Never* to 3 = *Always*.

Michigan Alcoholism Screening Test (MAST)

The Michigan Alcoholism Screening Test (MAST) is a measure of AUD symptoms, one of our two moderators. It is one of the most widely used assessments for alcohol misuse, with 25 items in a self-administered questionnaire (Selzer, 1971). A study from 2000 found that there was a significant ($Z = 17.88, p < .0001$) degree of validity as demonstrated by the survey in several psychiatric settings (Teitelbaum & Mullen, 2000). The 25 items were rated on a dichotomous scale of 1=Yes, 0=No,

with higher scores correlating with increased manifestation of AUD symptoms. An example item is: "Has your drinking ever resulted in your being hospitalized in a psychiatric ward?" (Selzer, 1971). See Appendix for additional sample items for all measures.

Hair Cortisol

As previously discussed, the mediator in our model is stress response, operationalized as hair cortisol levels (pg/mg hair). Participants received a study package in the mail with foil and visual instructions on how to collect a hair sample from the nape of the neck. Once wrapped in foil, the hair samples were sent back to be analyzed. Hair cortisol was extracted with acetone/methanol, dried under nitrogen, and analyzed using Salimetrics HS Cortisol ELISA kits.

Statistical Analysis

We first looked at simple regression analyses between PTSD severity and the predictor/moderating variables (trauma exposure, MDD symptoms, and AUD symptoms) to assess if there was a significant relationship between these before completing further analyses. Then, a moderated mediation analysis was used to explore the association between trauma exposure and PTSD outcomes, as well as the indirect effect of hair cortisol on that direct relationship. Additionally, the moderation was examined by looking at whether the indirect effect of hair cortisol changed for those who were one standard deviation above or below the mean in relation to both MDD and AUD symptomology. In order to evaluate the statistical significance of the model, the *PROCESS* macro was imported into *R Studio* Version 1.4.1106. *PROCESS* is a function that allows for testing of a linear interaction between the predictor and the moderator in a model of the outcome variable (Hayes, 2017). To test for the moderation, it uses process modeling to estimate the influence of the direct and indirect pathways of the predictor and outcome (Hayes, 2017). *PROCESS* uses bootstrapping, a statistical approach that increases the validity of results from small sample sizes by resampling with replacement from the original distribution to create a handful of simulated samples, reducing confounds by mimicking the sampling process (LaFontaine, 2021).

PROCESS Model 7 was used to test our model, as it tests the moderated mediation of both the c' path (as shown in figure 1), and the a path (as shown in Figure 2). Thus, we examined the following relationships: (a) the direct effect of trauma exposure on PTSD outcomes, (b) the effect of trauma exposure on hair cortisol levels, (c) the effect of hair cortisol levels on PTSD outcomes, (d) the indirect effect of trauma exposure on PTSD outcomes through hair cortisol, and (e) the interaction between MDD/AUD comorbidity and hair cortisol. Both age and gender were included as covariates in the model, as the literature has shown differences in many forms of psychopathology, including PTSD, across different ages (Karel et al.,

2012), and among different genders (Rosenfield & Mouzon, 2013).

Models

Figure 1

Model of the Direct Relationship of the Predictor Variable on the Outcome Variable.

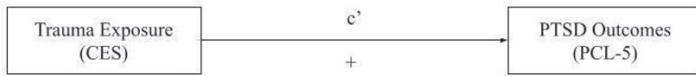


Figure 2

Model of Moderated Mediation of MDD Symptoms.

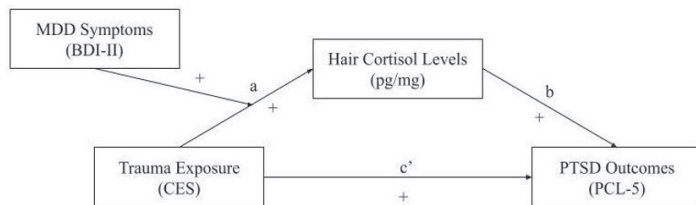
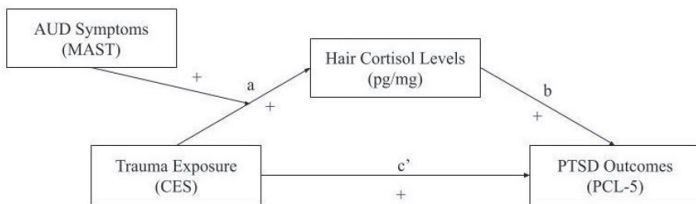


Figure 3

Model of Moderated Mediation of AUD Symptoms.



Results

Descriptive Statistics

Preliminary descriptive statistics showed that on average, our sample of veterans reported lower levels of trauma exposure on a scale of 0 to 15 ($M = 4.08$, $SD = 4.42$). Additionally, cortisol levels were low on average ($M = 13.29$ pg/mg, $SD = 10.94$), whereas the literature has reported that cortisol levels can reach anywhere up to 150 pg/mg in stressed individuals (Suavé et al., 2007). BDI-II scores indicate mild depression on average in our sample, ($M = 17.92$, $SD = 11.25$) however, the standard deviation was large and the scores ranged from 2 to 42, indicating that some non-depressed and some severely depressed individuals were likely represented in our

sample. Additionally, the MAST indicated a low incidence of AUD ($M = 4.05$, $SD = 5.24$), where a total of 6 or higher indicates hazardous drinking or dependence. Finally, Our PCL-5 data indicated that there might be some individuals with PTSD in our sample ($M = 25.62$, $SD = 18.80$), with the possible range of the scoring being from 0 to 80.

Table 2

Means, Standard Deviations, and Ranges of Measures

Measure	<i>M</i>	<i>SD</i>	Observed Range	Possible Range
CES	4.08	4.42	[0, 15]	[0, 15]
Hair Cortisol	13.29	10.94	[2.93, 49.84]	N/A
BDI-II	17.92	11.25	[2, 42]	[0, 63]
MAST	4.05	5.24	[0, 20]	[0, 22]
PCL-5	25.62	18.80	[0, 69]	[0, 80]

Note. *M* and *SD* are used to represent mean and standard deviation, respectively.

Linear Regression

In order to confirm a direct relationship between the predictor and outcome variable, and to look into the relationship between the other variables in the model, a few simple regression analyses were done before completing the moderated mediation. First, as seen in figure 4, the direct effect of trauma exposure on PTSD symptoms was significant ($p < .05$), and the results of the regression indicate the model accounts for 15.7% of the variance ($F(1,34) = 6.906$). This indicates a moderate, positive relationship between trauma exposure and PTSD outcomes. Additionally, as seen in figure 5, the relationship between PTSD severity and MDD severity was analyzed, and the results of the regression indicate that the model accounts for 52.3% of the variance, which was significant ($F(1,34) = 40.51$, $p < .01$). This indicates a strong, positive relationship between PTSD and MDD severity. Finally, as seen in figure 6, the results of the regression indicated that the model accounted for 17.2% of the variance, which was also significant ($F(1,34) = 7.705$, $p < .01$). This indicates a moderate, positive relationship between AUD and PTSD outcomes. The results of all three regression analyses are outlined in table 3 below. Judging by the significant association between the variables in our model, we saw it fit to proceed with the moderated mediation.

Figure 4

Regression Plot of CES Score Plotted Against PCL Score

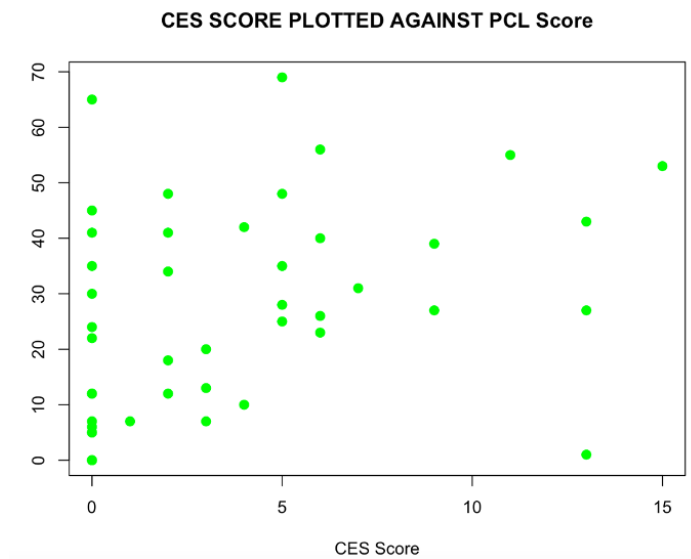


Figure 6

Regression Plot of MAST Score Plotted Against PCL Score

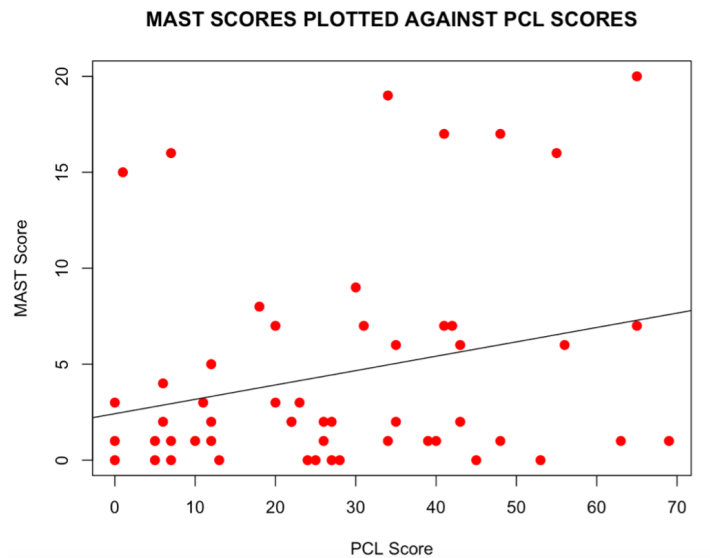


Figure 5

Regression Plot of BDI Score Plotted Against PCL Score

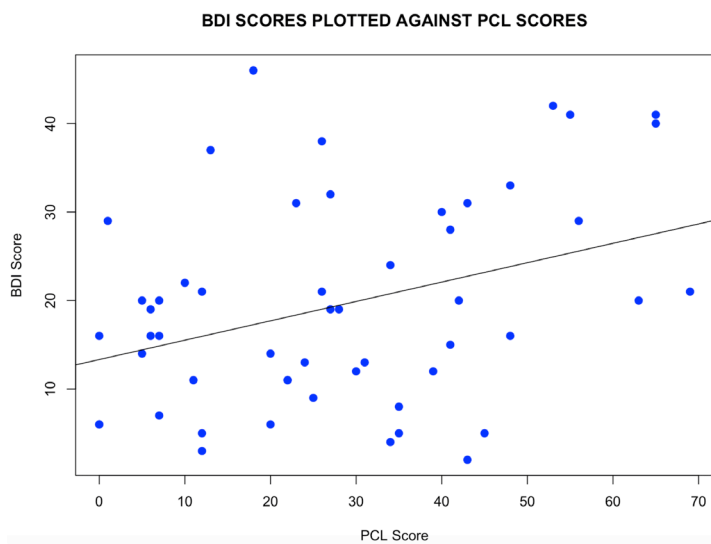


Table 3

Simple Regression Results using PCL Score as Outcome

Predictor	<i>b</i>	<i>b</i> 95% CI [LL, UL]	<i>beta</i>	<i>beta</i> 95% CI [LL, UL]	<i>sr</i> ²	<i>sr</i> ² 95% CI [LL, UL]	<i>r</i>	Fit
(Intercept)	3.96	[-4.15, 12.07]						
BDI Score	1.21**	[0.82, 1.59]	0.72	[0.49, 0.95]	.52	[.28, .66]	.72**	$R^2 = .523^{**}$ 95% CI [.28, .66]
(Intercept)	19.58**	[12.44, 26.73]						
MAST Score	1.49**	[0.40, 2.58]	0.42	[0.11, 0.72]	.17	[.01, .37]	.42**	$R^2 = .172^{**}$ 95% CI [.01, .37]
(Intercept)	18.73**	[10.96, 26.50]						
CES Score	1.69*	[0.39, 2.99]	0.40	[0.09, 0.70]	.16	[.01, .36]	.40*	$R^2 = .157^*$ 95% CI [.01, .36]

Note. A significant *b*-weight indicates the beta-weight and semi-partial correlation are also significant. *b* represents unstandardized regression weights. *beta* indicates the standardized regression weights. *sr*² represents the semi-partial correlation squared. *r* represents the zero-order correlation. LL and UL indicate the lower and upper limits of a confidence interval, respectively.

* indicates $p < .05$. ** indicates $p < .01$.

Moderated Mediation

Our model examined the mediating effect of cortisol levels on the relationship between trauma exposure and PTSD severity, and the effect of the moderating variable of comorbidity (either MDD or AUD) on the outcome by way of the effect on the mediating variable. The direct effect of trauma exposure on PTSD severity was significant ($B=2.63$, $SE=1.0575$, $p=.018$). This indicates that trauma exposure is positively associated with PTSD severity, regardless of the amount of hair cortisol (Figures 7 and 8).

Additionally, in the model exploring moderation by MDD, the severity of MDD was not significantly correlated with hair cortisol levels ($B=0.3462$, $SE=0.2124$, $p=.11$). This indicates that the mediating effect of hair cortisol on the relationship between trauma exposure and PTSD severity was not moderated by MDD severity. However, the interaction effect of MDD severity and trauma exposure on hair cortisol levels was significant ($B=-0.4049$, $SE=0.1704$, $p=0.02$). This indicates that the mediating effect of hair cortisol on the relationship between trauma exposure and PTSD severity was significant based on the negative interaction of MDD and trauma exposure (Figure 7).

The same model was run with AUD severity as the moderator instead of MDD. However, in this case, none of the relationships were significant, indicating that AUD does not moderate the relationship between trauma exposure and

PTSD severity, as mediated by hair cortisol levels (Figure 8).

Interestingly, there was one unexpected significant effect in the model. When looking at the conditional effects of trauma at different values of the MDD moderator, we found a significant effect among those with BDI scores one standard deviation below the mean (-11.25). When the value for the BDI was low, there was a significant relationship between CES score and PCL score, $B=5.26$, 95% CI [1.21, 9.31], $t=2.64$, $p=.0125$. This indicates that BDI does have some significance as a moderator in this relationship, however the relationship was not significant at one standard deviation above the mean: $B=-3.85$, 95% CI [-7.93, 0.234], $t=-1.92$, $p=.0638$.

Figure 7

Model of Moderated Mediation (MDD mediator)

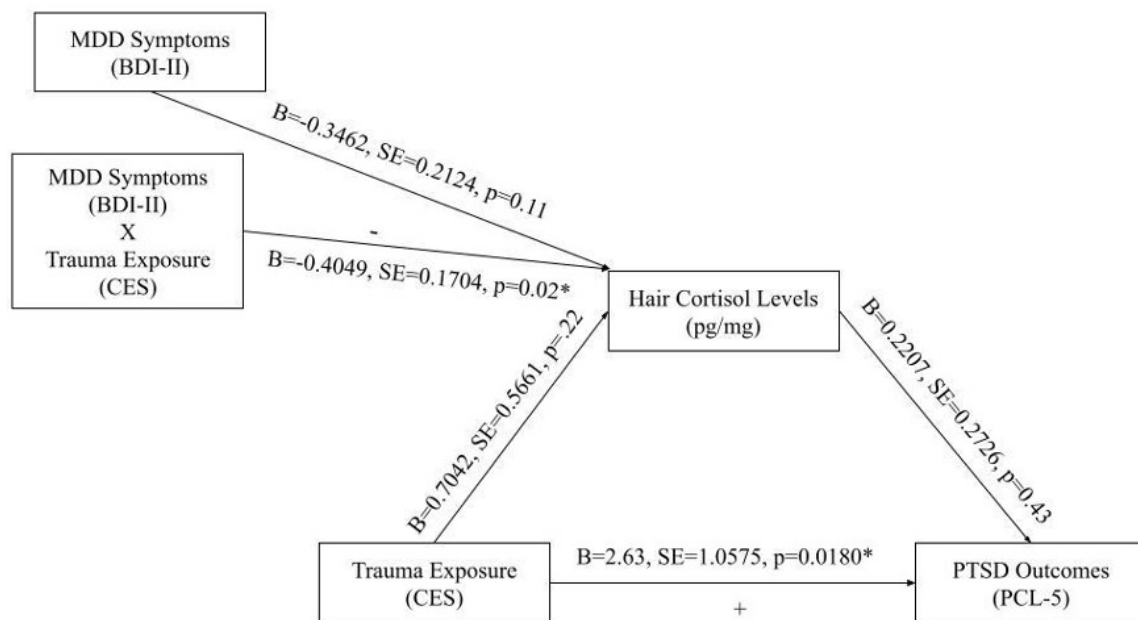
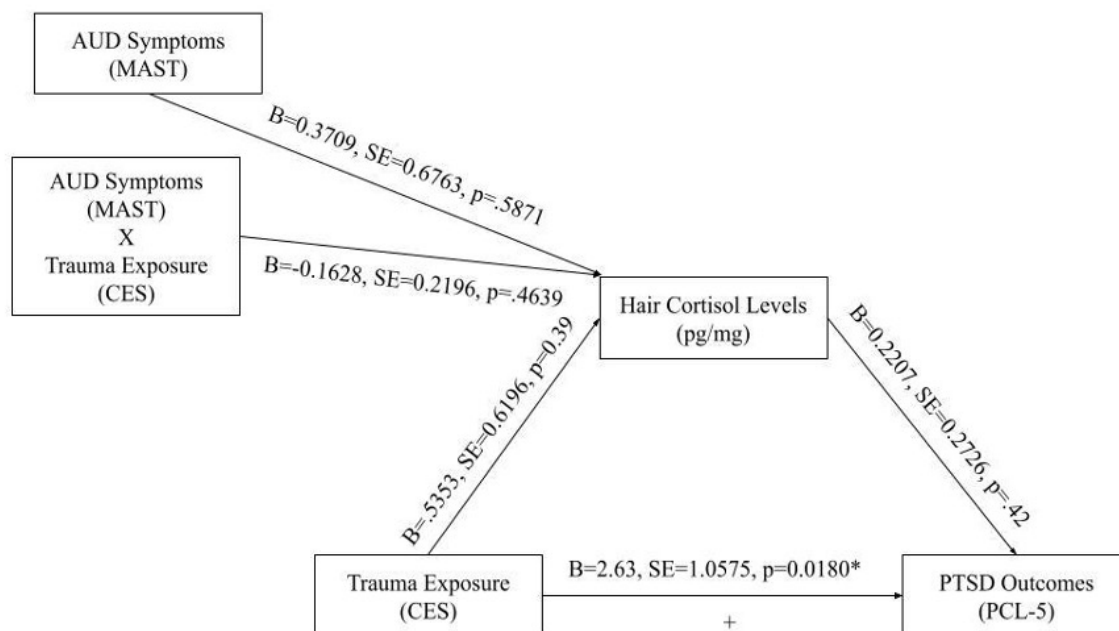


Figure 8

Model of Moderated Mediation (AUD mediator)



Discussion

In this study, we examined the relationship between trauma exposure and PTSD outcomes, and how this relationship is influenced by an increase in cortisol. Furthermore, we investigated whether the strength of the relationship between trauma exposure and hair cortisol was strengthened by any pre-existing comorbidities (specifically with MDD and AUD). Our findings showed that, as expected, the direct effect of trauma exposure on PTSD severity was significant, and that the two were positively correlated. However, the mediating effect of hair cortisol was not significant and does not explain the relationship between the predictor and outcome variables. Yet, we did find a significant interaction of comorbid MDD and trauma exposure on the path from trauma exposure to hair cortisol levels. This indicates that the interaction of these factors does influence the model, and that MDD comorbidity does, in fact, predict the effect of trauma exposure. A similar effect was not found for comorbid AUD.

Our model indicates that, on its own, hair cortisol is not a useful predictor of PTSD outcomes. There have been instances within the literature that support the usefulness of cortisol, as well as the lack of validity for cortisol, as a predictor for psychiatric outcomes. While some studies have shown that higher levels of trauma exposure, as well as PTSD symptoms were correlated with lower long-term integrated cortisol secretion (Steudte-Schmiedgen et al., 2015), our study would appear to support the contrary opinion. Our study's findings aligned more closely with those that did not find a significant relationship, as the results provide little evidence for the predictive value of pre-treatment hair cortisol concentrations for clinical symptom change over the course of an inpatient treatment for PTSD (Hummel et al., 2021). None of the direct pathways leading to or from hair cortisol were significant, and this supports the notion that it does not reliably predict PTSD severity. Alternatively, there are indications that the presence of MDD comorbid with the PTSD may affect the strength of the relationship between trauma exposure and PTSD severity, with lower depressive scores associated with a stronger trauma to PTSD correlation. This gives us insight into how, moving forward, future studies could test the effectiveness of cortisol as a biomarker for various disorders.

When considering the practical implications of this study, our lack of significant results regarding hair cortisol calls for further research into the use of cortisol as a biomarker—as the conflicting research warrants a deeper analysis into its ability to indicate the presence of one or more mental health disorders. Future studies could expand investigations into the relationship between hair cortisol and other types of trauma exposures, including those not related to combat situations. This could be physical, emotional, or sexual trauma. Focusing on populations other than veterans would not only contribute to PTSD research but could also serve to increase the external validity of the current study. Future studies could also conduct measures in person as opposed to through online

surveys, allowing them to use highly regarded clinician rated scales such as the CAPS-5 for PTSD, the C-SSRS for suicidality, the AUDIT for alcohol use, or the more in-depth SCID for all major DSM-5 diagnoses. Conducting these surveys in person would also minimize the risk for attrition, as it is easier to ensure that participants complete all of the surveys when a researcher is present.

One result our study did confirm was the significance of the relationship between trauma exposure and PTSD severity. Trauma exposure is the primary requirement for a PTSD diagnosis, and veterans have inherently experienced more trauma than most citizens. Not only do they often witness violence, but they can also experience violence themselves, and the strict discipline of the military can cause trauma to its active-duty service members. Thus, this is an important population to investigate when attempting to understand PTSD and its treatment. Observing this well-known relationship between trauma exposure and PTSD in our study suggests that our design had good convergent validity and had the prospect of detecting the hypothesized mediating and moderating effects if they were operating.

There are some factors that may have contributed to the lack of significant effects in our a, b, and AUD moderation paths, and these are mainly concerns of external validity. This study was a secondary analysis, meaning that the data being analyzed was collected as part of a separate study. Thus, it would be beneficial to replicate this study with not just a larger sample size, but also a much more diverse sample. In this case, it is important to clarify that diversity applies to diversity in gender, as well as race and ethnicity. Given that the overall sample was both small ($n=35$) and homogeneous (80% male and 79% white), replicating the study with a larger, more diverse sample size could improve the external validity and power of the results. Additionally, the sample at hand was composed entirely of United States veterans, and the population of interest in this study was veterans who experienced trauma in combat. Thus, the study cannot be extrapolated to other trauma experiences aside from combat exposure, or veterans who did not serve in the United States.

Finally, it is important to address the attrition in the sample. Of the 53 who partially completed the study, just 35 participants finished all the measures, a reduction by almost half. In completing the Qualtrics surveys, it is likely that some participants stopped part of the way through, thus only providing data for some of our measures. Others simply did not send a hair sample, and thus, their survey data was not usable. This in part contributed to the small sample size, and future studies should attempt to minimize the rate of attrition.

Conclusion

This analysis contributes to the literature on treatment and prevention of PTSD by examining the relationship between trauma exposure, hair cortisol, and PTSD outcomes while also examining the moderating role of various comorbidities

(specifically, MDD and AUD) in a veteran population that is at much higher risk for development of mental health disorders. Veterans in the United States face many barriers to accessing mental health resources, leading to an even higher risk of developing MDD, AUD, and PTSD (among other disorders). While many treatments exist for the civilian population, few resources directly address veterans. Hotlines, response teams, and inpatient units are not readily available at most VA Hospital and Health Systems, and this barrier to treatment is, in part, due to a lack of insurance coverage and affordable healthcare (Hester, 2017). Hopefully, through identifying a valid and reliable biomarker for PTSD, treatment of veterans will be covered by more insurance agencies, and agencies such as the VA and other government programs will obtain increased funding. The results of our study indicate that hair cortisol may not be a strong or reliable biomarker for identifying PTSD, and further investigations in overstimulation and passivation of the HPA axis could give insight into why this is so.

Our work also highlighted the importance of considering comorbidities in PTSD research. Comorbidities are increasingly common and notoriously difficult to treat, and research on prevention and risk factors is necessary to help those who are affected or at risk. It is crucial that researchers in this field continue to investigate the best biomarkers for various mental health disorders, and that risk factors for increased severity and comorbidity are considered as well. The literature for biomarkers of psychological disorders is relatively new and there is much to learn. Given the conflicting reports of cortisol in varying mental health disorders (Hummel et al., 2021; Petrowski et al., 2020; Stephens & Wand, 2012), future studies could focus on how hair cortisol levels change over time in those with PTSD, such as before and after trauma exposure. This could give insight into how cortisol changes as a result of trauma and offer a benchmark for comparison. Additionally, future studies could analyze and compare the hair cortisol levels of non-comorbid disorders. For example, measuring and comparing the hair cortisol of those with a PTSD diagnosis versus those with an MDD or AUD diagnosis could give insight into how these disorders affect each other, and subsequently, how varying levels of cortisol may predict different comorbidities. In a country where nearly 75% of the population has experienced a traumatic event, researching the mechanisms by which trauma leads to PTSD is crucial. Identifying an objective laboratory-based diagnostic test for PTSD could help clinicians assess and treat patients more rapidly and efficiently.

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Appendix

Table A1

BDI-II Item Examples

1. Sadness 0. I do not feel sad. 1. I feel sad much of the time. 2. I am sad all the time. 3. I am so sad or unhappy that I can't stand it.
2. Pessimism 0. I am not discouraged about my future. 1. I feel more discouraged about my future than I used to be. 2. I do not expect things to work out for me. 3. I feel my future is hopeless and will only get worse.
3. Past Failure 0. I do not feel like a failure. 1. I have failed more than I should have. 2. As I look back, I see a lot of failures. 3. I feel I am a total failure as a person.
4. Loss of Pleasure 0. I get as much pleasure as I ever did from the things I enjoy. 1. I don't enjoy things as much as I used to. 2. I get very little pleasure from the things I used to enjoy. 3. I can't get any pleasure from the things I used to enjoy.
5. Guilty Feelings 0. I don't feel particularly guilty. 1. I feel guilty over many things I have done or should have done. 2. I feel quite guilty most of the time. 3. I feel guilty all of the time.

Table A2

CES Item Examples

1. Did you ever go on combat patrols or have other dangerous duties?				
1. No	2. 1-3 times	3. 4-12 times	4. 13-50 times	5. 51+ times
2. Were you ever under enemy fire?				
1. Never	2. <1 month	3. 1-3 months	4. 4-6 months	5. 7+ months
3. Were you ever surrounded by the enemy?				
1. No	2. 1-2 times	3. 3-12 times	4. 13-25 times	5. 26+ times
4. What percentage of the soldiers in your unit were killed (KIA), wounded or missing in action (MIA)?				
1. None	2. 1-25%	3. 26-50%	4. 51-75%	5. 76% or more
5. How often did you fire rounds at the enemy?				
1. Never	2. 1-2 times	3. 3-12 times	4. 13-50 times	5. 51+ times

Table A3

MAST Item Examples

1. Do you feel you are a normal drinker? (By normal we mean you drink less than or as much as most other people.)	Yes	No
2. Have you ever awakened the morning after some drinking the night before and found that you could not remember a part of the evening?	Yes	No
3. Does your wife, husband, a parent, or other near relative ever worry or complain about your drinking?	Yes	No
4. Can you stop drinking without a struggle after one or two drinks?	Yes	No
5. Do you ever feel guilty about your drinking?	Yes	No

Table A4

PCL-5 Item Examples

In the past month, how much were you bothered by:
1. Repeated, disturbing, and unwanted memories of the stressful experience? Not at all A little bit Moderately Quite a bit Extremely
2. Repeated, disturbing dreams of the stressful experience? Not at all A little bit Moderately Quite a bit Extremely
3. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)? Not at all A little bit Moderately Quite a bit Extremely
4. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)? Not at all A little bit Moderately Quite a bit Extremely
5. Guilty Feelings Not at all A little bit Moderately Quite a bit Extremely