AUDITORY HALLUCINATIONS IN THE CONTEXT OF PAST TRAUMA: THE ROLE

OF POSTTRAUMATIC STRESS SYMPTOMS AND POTENTIAL OF TRAUMA-

FOCUSED PSYCHOLOGICAL THERAPIES AS A NOVEL TREATMENT APPROACH.

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Abstract

Auditory hallucinations (experiences of hearing a noise or voice in the absence of a corresponding external stimulus) are common across a range of psychiatric diagnoses and are often (but not always) associated with significant distress and disability. The current best practice psychological therapy for psychotic experiences, cognitive behavioural therapy for psychosis, has only shown small to moderate effects for auditory hallucination related outcomes. A symptom-focused approach that targets empirically derived mechanisms underpinning auditory hallucinations may improve therapy efficacy.

One candidate causal pathway that may inform therapy development is that of trauma and adversity. There is mounting evidence that traumatic life events (such as childhood abuse and neglect) play a causal role in auditory hallucinations. Theory and research indicate that posttraumatic stress disorder (PTSD) symptoms, such as trauma memory intrusions, hyperarousal, and avoidance may be important psychological mechanisms in the relationship between trauma and auditory hallucinations. Specifically, contemporary trauma-informed cognitive behavioural theories of auditory hallucinations have posited that some auditory hallucinations may be trauma memory intrusions that are encoded in a particularly decontextualised form. This offers promise for intervention development, since there are well-evidenced psychological therapies for PTSD.

The broad aim of this programme of research was to explore the role of PTSD symptoms and trauma memory processing as potential psychological mechanisms involved in auditory hallucinations, and as a potential target for treatment using trauma-focused psychological therapies. Specifically, the research aimed to further elucidate the role of PTSD symptoms in auditory hallucinations, moving beyond cross-sectional data by exploring the micro-longitudinal, moment-to-moment relationship between PTSD symptoms and auditory hallucinations. Secondly, this programme of research specifically aimed to examine the

feasibility, acceptability, and potential effects of trauma-focused psychological therapies (that already have proven efficacy in treating PTSD symptoms) for trauma-related auditory hallucinations.

Study One utilised ecological momentary assessment to examine micro-longitudinal relationships between PTSD symptoms and auditory hallucinations. Results indicated that trauma memory intrusions had momentary associations with the occurrence of auditory hallucinations. This relationship was stronger and more enduring for those with a direct link between their auditory hallucination content and their index traumatic event.

Study Two involved a systematic review of studies that have used trauma-focused therapies to treat comorbid PTSD in populations with schizophrenia spectrum or psychotic disorders. A meta-analytic synthesis provided an estimate of the secondary effects of these therapies on psychotic symptoms, finding small significant post treatment effects on positive symptoms (not maintained at follow up). Effects on auditory hallucinations were small and nonsignificant and were based on limited data.

Study Three was a pilot trial examining the feasibility, acceptability, and potential effects of an exposure-based trauma-focused therapy (imaginal exposure) that specifically targeted trauma-related auditory hallucinations. Participants reported high levels of satisfaction; however temporary distress and symptom exacerbation were common and unmanageable for some. There was a large reduction in auditory hallucination severity, but individual response was highly variable.

Overall, thesis findings provide support for the theory that (some) auditory hallucinations have an intricate link to trauma memory intrusions. Exposure-based trauma focused therapies may be an effective intervention for some people, but temporary distress and symptom exacerbation are common and may be difficult to tolerate for a minority.

Further research is needed to definitively assess efficacy and to identify clinical and contextual factors that influence therapy response and tolerability.

Acknowledgements

Declaration

I, the candidate, declare that the contents of this thesis:

1. Contains no material which has been accepted by me for the award of any other degree at any other university or equivalent institution.

2. To the best of my knowledge, contains no material previously published or written by another person except where appropriate reference is made in the thesis.

3. Discloses the relative contributions of the authors on work that is based on joint research or publications.

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Signed

Dated: 24th October, 2019.

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List of Peer Reviewed Publications During Candidature

Brand, R.M., Hardy, A., Bendall, S., and Thomas, N. (in press). A tale of two outcomes: Remission and exacerbation in the use of trauma-focused imaginal exposure for trauma-related voice-hearing. Key learnings to guide future practice. *Clinical Psychologist.*

Brand, R.M., Thomas, N. & Murray, G. (in press). The assessment of people with psychotic and bipolar disorders. In Selbom, M. & Suhr, J. (eds) Handbook of Clinical Assessment and Diagnosis, Cambridge University Press.

Varker, T., **Brand, R.M**., Ward, J., Terhaag, S. & Phelps, A. (2018). Efficacy of synchronous telepsychology interventions for people with anxiety, depression, posttraumatic stress disorder, and adjustment disorder: A rapid evidence assessment. *Psychological Services*, ePub ahead of print, doi: 10.1037/ser0000239.

Brand, R.M., McEnery, C., Bendall, S., Rossell, S. & Thomas, N. (2018) Do trauma-focused psychological interventions have an effect on psychotic symptoms? A systematic review and meta-analysis. *Schizophrenia Research, 195*, 13-22. doi: 10.1016/j.schres.2017.08.037.

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Brand, R.M., Chisholm, K., Terhaag, S., Lau, W., Forbes, D., Holmes, A., O'Donnell, M. (2017) Understanding the early support needs of survivors of traumatic events: The example of severe injury survivors. *Psychological Trauma: Theory, Research, Practice and Policy, 10(3),* 376-385. doi: 10.1037/tra0000274.

Forbes, D., O'Donnell, M., **Brand, R.M**., Korn, S., Creamer, M., McFarlane, A., Sim, M., Forbes, A. & Hawthorne, G. (2016) The long term mental health status of Australian

peacekeepers: prevalence and predictors of psychiatric disorder, *British Journal of Psychiatry Open, 2* (1) 32-37. doi: 10.1192/bjpo.bp.115.001321.

List of Conference Presentations During Candidature

Brand, R.M., Bendall, S., Hardy, A., Rossell, S., Thomas, N. (2019) A pilot trial of imaginal exposure therapy for people with trauma-related voices: feasibility, acceptability and potential effects. [Oral Presentation]. Early Career Hallucination Researchers Annual Meeting, Durham, UK.

Brand, R.M., Bendall, S., Rossell, S., Meyer, D., Hardy, A. & Thomas, N. (2019). The moment-to-moment relationship between auditory hallucinations and posttraumatic stress disorder symptoms in the flow of daily life. [Oral Presentation]. Swinburne University Centre for Mental Health Research Symposium, Melbourne, Australia.

Brand, R.M., Bendall, S., Rossell, S., Meyer, D., Hardy, A. & Thomas, N. (2019). The relationship between voice hearing and posttraumatic stress disorder symptoms in daily life: An ecological momentary assessment study [Oral Presentation]. World Congress of Behavioral and Cognitive Therapy. Berlin, Germany.

Brand, R.M., Bendall, S., Hardy, A., Rossell, S., Thomas, N. (2019) A pilot trial of imaginal exposure therapy for people with trauma-related voices: Results, lessons learnt, and questions to inform the development of trauma-focused therapies for psychosis. [Oral Presentation]. World Congress of Behavioral and Cognitive Therapy. Berlin, Germany.

Brand, R.M., Bendall, S. (2018) Understanding and treating posttraumatic stress symptoms in people with psychosis. Invited webinar for the Australian Psychological Society Psychosis Special Interest Group.

Brand, R.M., McEnery, C., Bendall, S., Rossell, S. & Thomas, N. (2018). Do trauma-focused psychological interventions have an effect on psychotic symptoms? A systematic

review and meta-analysis [Oral presentation]. World Psychiatric Association Thematic Congress, Melbourne, Australia.

Harrop, C., Lobban, F., Ellett, L., & **Brand, R.M**. (2016). Young people with psychosis want friends and romantic relationships – Can professionals help? IEPA 10, Early Intervention in Mental Health, Milan, Italy.

List of Grants and Awards During Candidature

Grants

2019: Early Career Hallucination Researcher Group Travel Grant $1300

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2015-2019: Swinburne University Postgraduate Research Award $82,788

Awards

2019: Royal Society of Victoria, Young Scientist Research Awards, 2nd place, Biomedical and Health Sciences Category.

PART I: BACKGROUND AND LITERATURE REVIEW

Chapter One: Introduction and Thesis Overview

1.1 Background

There is a growing body of evidence suggesting that traumatic and adverse life events play a causal role in psychotic symptoms, including auditory hallucinations (Varese et al., 2012). Indeed, such events represent one of the most robust environmental predictors of psychosis (Belbasis et al., 2018). A number of psychological mechanisms have been implicated in the relationship between trauma and auditory hallucinations (Williams, Bucci, Berry, & Varese, 2018); one strand of this literature implicates posttraumatic stress disorder (PTSD) symptomatology and trauma memory processing in the genesis and maintenance of trauma-related auditory hallucinations (Hardy, 2017; Steel, 2015). The majority of evidence in this area is cross-sectional and there is a need for research that can more robustly assess dynamic moment-to-moment relationships and strengthen causal inferences. Additionally, there is currently a lack of research into psychological therapies for auditory hallucinations that address the role of trauma and trauma-related mechanisms. Psychological therapies that can address the role of trauma in auditory hallucinations could provide a much-needed new avenue in treatment approaches for auditory hallucinations (Thomas et al., 2014).

1.2 Overall aims of the thesis and included studies

The overarching aim of this thesis was to explore the role of PTSD symptoms and trauma memory processing as potential psychological mechanisms involved in auditory hallucinations, and as a potential target for treatment. This aim was addressed using a multi method approach, including: a comprehensive literature

review (including a published opinion piece), three empirical studies and a clinical reflection using case study material.

Firstly, a study using ecological momentary assessment (EMA) explored whether PTSD symptoms predict auditory hallucinations in everyday life, providing novel data regarding dynamic moment-to-moment relationships. Secondly, a meta-analysis of trauma-focused psychological therapies delivered to treat comorbid PTSD in psychosis populations was used to examine the secondary effects of these therapies on psychotic symptoms. Finally, a pilot treatment study provided a preliminary investigation of the feasibility, acceptability and effectiveness of a psychological therapy focused on psychological processes postulated to underlie the trauma–auditory hallucination link. This study paves the way for larger studies that can use an interventionist–causal framework to provide experimental evidence for causality in the relationship between posttraumatic stress symptoms, trauma memory processing and auditory hallucinations.

1.3 Overview of the thesis

The thesis is presented as follows. Chapter Two provides an overview of the nature of auditory hallucinations and putative psychological mechanisms involved. This includes a review of the status of current psychological therapies, with a focus on the shortcomings of this literature to date and the potential of *process-based* therapies that target specific psychological processes implicated in auditory hallucinations. Chapter Three narrows the focus of the literature review to the area of specific interest in this thesis and examines whether past trauma and adversity play a causal role in psychotic experiences. This includes an exploration of postulated psychological mechanisms in the trauma-auditory hallucination relationship. Chapter Four provides a more in depth exploration of the role of PTSD symptomatology in trauma-related

auditory hallucinations and of the possibility that auditory hallucinations are a type of posttraumatic intrusion caused by decontextualised episodic memories. Chapter Five presents the first publication from this PhD, which is an opinion piece regarding the need for a methodological shift in investigating the role of PTSD symptoms in auditory hallucinations. Chapter Six provides a summary of the literature review and outlines the overall aims of the empirical studies included in the thesis. Chapter Seven then gives an overview of the methods for each empirical study as well as discussing key methodological decisions that are not addressed in detail in the peer reviewed publications. Chapter Eight presents the second publication from this thesis, which outlines the findings of the EMA study of the relationship between PTSD symptoms and auditory hallucinations in daily life. Chapter Nine is the third publication, a systematic review and meta-analysis exploring whether trauma-focused therapies have an effect on psychotic symptoms. Chapter Ten includes the fourth publication, presenting the main quantitative findings from the pilot study of a trauma-focused therapy for trauma-related auditory hallucinations. Chapter Eleven is the final publication from the thesis, which is a clinical reflection on the use of trauma-focused therapies for trauma-related auditory hallucinations, comparing and contrasting two case illustrations from the pilot study; one for whom the therapy was tolerable and effective, and one for whom it was not. Finally, chapter Twelve provides an overall discussion of the findings from the thesis, synthesising all of the evidence from all of the empirical work to reflect on conclusions and implications as well as on limitations in the methods used.

1.4 Context to the thesis

This thesis presents a sequence of interrelated empirical studies that, in combination, address the overarching aim of the programme of research. The format

of the thesis is *by publication* and includes three manuscripts that have been accepted

for publication in peer reviewed journals and two manuscripts that are currently under

review. The incorporation of these manuscripts in the thesis means that there is some

unavoidable repetition, particularly in the introduction sections of the peer reviewed

publication manuscripts. Despite this repetition, each peer reviewed publication

manuscript outlines a study that is unique in its aims, design, and method. The

methods of each empirical study are also outlined in the peer reviewed publication

manuscripts, however, due to word limits for such manuscripts, exhaustive

descriptions of study methods are not possible. As such, Chapter Seven of the thesis

provides supplementary details regarding the specific methods used in the three

empirical studies. Of note, UK English spelling is used throughout the thesis, in

accordance with university requirements. The empirical studies were all conducted

and written up within the set period of candidature and in accordance with ethical

requirements. Ethical approval certificates are presented in Appendix I.

<center>**Chapter Two: Auditory Hallucinations**</center>

2.1 Definition

      Hallucinations have been defined as "any percept-like experience that (a) occurs in the absence of an appropriate stimulus, (b) has the full force or impact of the corresponding actual (real) perception, and (c) is not amenable to direct and voluntary control by the experiencer." (Slade & Bentall, 1988, pp. 23). Similarly, the Diagnostic and Statistical Manual of Mental Disorders (DSM 5, American Psychiatric Association, 2013) defines hallucinations as "perception-like experiences that occur without an external stimulus. They are vivid and clear, with the full force and impact of normal perceptions, and not under voluntary control" (pp. 87). Hallucinations can occur across all sensory modalities, including visual, auditory, olfactory, or tactile experiences. Auditory hallucinations are the most prevalent hallucinatory experience (McCarthy-Jones et al., 2017) and are the main focus of this thesis. Auditory hallucinations are generally defined as the experience of hearing a voice or sound in the absence of a corresponding external stimulus, however phenomenological studies have provided a more nuanced understanding, showing that the term actually encompasses a broad spectrum of experiences ranging from auditory imagery (mental representations based on auditory perceptions), to intrusive and vivid thoughts with a sense of 'otherness', through to more frank experiences of hearing complex sounds and voices (Jones & Luhrmann, 2016; Woods, Jones, Alderson-Day, Callard, & Fernyhough, 2015). Nonverbal auditory hallucinations can involve hearing sounds such as music, ringing, animal sounds, clicks, humming, and water (McCarthy-Jones et al., 2014). Auditory-verbal hallucinations are often reported to be similar to the experience of hearing others speak, though sometimes experienced as being unlike real voices, or as 'soundless' voices in which a message or meaning is communicated,

but is not experienced as being 'heard' as a voice (Larøi et al., 2012). Auditory-verbal hallucinations are the most common auditory hallucination, being present in the majority of people with auditory hallucinations in psychiatric populations (McCarthy-Jones et al., 2014; Nayani & David, 1996). Nonverbal hallucinations have been found to occur in approximately one third of the psychiatric population who experience auditory hallucinations, most commonly in conjunction with auditory verbal hallucinations (McCarthy-Jones et al., 2014).

2.2 Prevalence

Despite historically being considered to be pathognomonic for schizophrenia spectrum disorders, auditory hallucinations have more recently been recognised to occur across many different psychiatric disorders, including schizophrenia (40- 80%, Larøi et al., 2012), major depressive disorder (5.4-40.6%, Toh, Thomas, & Rossell, 2015), bipolar affective disorder (23%, Upthegrove et al., 2015), posttraumatic stress disorder (50%, Anketell et al., 2010), borderline personality disorder (46%, Kingdon et al., 2010), and dissociative identity disorder (87%, Ross et al., 1990). The phenomenology of auditory hallucinations also appears to be similar across different diagnostic groups (Waters & Fernyhough, 2017). In addition to conceptualising auditory hallucinations transdiagnostically, the last twenty years has seen a shift from the view of auditory hallucinations as a categorical and pathological experience (only occurring in psychiatric disorders), to an understanding that they in fact lie on a continuum of 'normal' experience. A large meta-analysis including 25 studies found the mean lifetime prevalence of auditory hallucinations was 9.6% (95% CI 6.7-13.6%) (Maijer, Begemann, Palmen, Leucht, & Sommer, 2018). Research suggests that the phenomenology of auditory hallucinations is largely similar in groups with and without a need for care (Johns et al., 2014). The main factors that seem to

differentiate those who seek treatment for their auditory hallucinations are: higher levels of negative content, lower perceived control, higher perceived power of the hallucination, longer duration, experiencing additional anomalies in sense of self and identity, and higher levels of distress and disruption to functioning (Johns et al., 2014). Major reviews in the area have found significant heterogeneity between studies examining prevalence rates of auditory hallucinations in the general population, highlighting methodological issues in this area (Beavan, Read, & Cartwright, 2011; Maijer et al., 2018). There have been inconsistencies in the way that auditory hallucinations have been measured and defined that appear to impact upon reporting rates; prevalence rates are higher in studies using self-report instruments (as opposed to clinician administered interviews) and less restrictive definitions (Beavan et al., 2011). As previously noted, phenomena that have been defined as auditory hallucinations encompass a broad spectrum of experiences (Woods et al., 2015) so the definitions and questions used to assess for auditory hallucinations are likely to have a large impact on reported prevalence rates.

2.3 Phenomenology

Although there is heterogeneity reported in the phenomenology of auditory hallucinations (Jones & Luhrmann, 2016; Woods et al., 2015), two large phenomenological studies have identified common characteristics (with a particular focus on auditory verbal hallucinations). Firstly, Nayani and David (Nayani & David, 1996) used a semi-structured questionnaire to explore the experiences of 100 people with psychotic disorders who had auditory hallucinations. Secondly, McCarthy- Jones et al. (McCarthy-Jones et al., 2014) analysed data from structured interviews conducted with 199 people with auditory hallucinations who had a range of diagnoses, including schizophrenia, affective disorders, and borderline personality

disorder (Copolov, Trauer, & Mackinnon, 2004). People often reported hearing multiple voices, with Nayani and David finding a mean of 3.2 voices per participant and McCarthy- Jones et al. reporting a mean of 4.3 voices. Both studies found that auditory hallucinations were experienced both internally and externally to the head. Participants were more likely to hear a male voice than a female voice and to hear voices at a normal conversational tone (though this varied, with many participants having soft/whispering voices or loud voices). In terms of the content of voices, 40% reported hearing some positive voices, but over 50% of people endorsed their voices to be persecutory, abusive, derogatory, threatening, or critical (McCarthy-Jones et al., 2014). In both of these samples the most common experience was that of very frequent commanding voices (Mackinnon, Copolov, & Trauer, 2004; Nayani & David, 1996).

2.4 Contemporary psychological theories of auditory hallucinations

Theory and research that attempts to understand the cause of auditory hallucinations has spanned many disciplines, with significant efforts to identify neuroanatomical, neurochemical, neurocognitive, and psychological factors that contribute to the genesis and maintenance of auditory hallucinations. This review focuses on psychological and neurocognitive theories of auditory hallucinations, given the topic of this thesis.

2.4.1 Self-monitoring

Neurocognitive models are unified by their conceptualisation of auditory hallucinations as internal mental events (thoughts, memories, imagery) that are experienced as coming from an external source (Bentall, 1990). Self-monitoring theories postulate that auditory hallucinations occur as a result of disruptions to normal processes involved in monitoring the intention to produce actions, leading to a

failure to recognise self-initiated actions as self-generated (Frith, 1992). This theory was initially focused on passivity experiences (in which self-initiated actions are experienced as being caused by external agents) but has since been applied to understanding auditory verbal hallucinations as a failure in the self-monitoring of inner speech (Jones & Fernyhough, 2007). This account is supported by experimental research that has demonstrated that people with psychotic disorders have poorer self-recognition than nonclinical controls and that this is more pronounced among people with auditory verbal hallucinations (Waters, Woodward, Allen, Aleman, & Sommer, 2010). However, Waters et al. (2010) also highlighted that their meta-analytic review of this research could not examine the possible confounding effects of general intellectual functioning or medication effects, due to a lack of data. General intellectual functioning has previously been suggested to be a confounding factor in the relationship between schizophrenia and self-monitoring deficits (Seal, Crowe, & Cheung, 1997). Despite strong evidence for an association between self-monitoring deficits and hallucinations, Waters et.al. (2010) also noted that a failure to recognise self-initiated events as self-generated is not sufficient to explain hallucinations, but that the process of misattribution of these events to an external source is also necessary.

2.4.2 Source monitoring

Source monitoring refers to a set of metacognitive processes involved in determining the origin of internal or external stimuli. Source monitoring is posited to involve a combination of *bottom up* perceptual processes and *top-down* cognitive processes (Johnson, Hashtroudi, & Lindsay, 1993). Source-monitoring accounts have suggested that hallucinations are not only caused by failures in self-monitoring, but that people prone to hallucinations also have specific cognitive biases towards the

misattribution of internal events to external sources (Bentall, 1990). This theory is supported by findings showing that auditory hallucinations tend to increase under conditions of high arousal and perceptual ambiguity, which are known to increase errors in judgement (Bentall, 1990). The importance of externalising biases in auditory hallucinations has also been supported by a meta-analytic review of experimental studies (Brookwell, Bentall, & Varese, 2013). However, these authors note that externalising biases might be involved in other symptoms that commonly covary with hallucinations (such as delusions, passivity experiences, and intrusive thoughts). Thus, studies that can methodologically or statistically control for comorbid symptoms are required to examine whether these biases are specific to hallucinations or are related to psychotic experiences more generally.

2.4.4 Hypervigilance to auditory threat

Slade and Bentall (1988) identified that the level of environmental stimulation plays a role in auditory hallucinations. Particularly, they posited that people who hallucinate are more likely to make errors in detecting a voice in background noise when the signal to noise ratio is low. They also identified that levels of arousal impacted on this process. Building upon this early work, Dodgson and Gordon (2009) outlined a theory that specifically describes the role of arousal in increasing errors in processing auditory stimuli in the presence of external noise. This theory describes how extreme emotional states can lead to hypervigilance to threat stimuli, which increases the likelihood of false positives in identifying meaningful threat material from background noise. This account has been supported by evidence finding that one common scenario in which auditory verbal hallucinations tend to occur is when attention is directed outwards, particularly in noisy contexts (Garwood, Dodgson, Bruce, & McCarthy-Jones, 2013). A small experimental study in a nonclinical sample

also found that high (induced) arousal increased auditory threat detection, particularly in those who were prone to auditory hallucinations (Dudley et al., 2014). Robust evidence for the hypervigilance theory of hallucinations is still lacking and further studies are needed to understand how levels of arousal impact upon auditory threat detection and whether this is an important mechanism in some auditory hallucinations.

2.4.3 Inhibition and contextual memory

Waters, Badcock, Michie, and Maybery (2006) proposed a neurocognitive model that suggests that auditory hallucinations are caused by the unintentional activation of memories and other mental representations. They theorise that a combination of impairments in intentional inhibition and contextual memory are critical to the experience of auditory hallucinations. Firstly, failures in inhibition of mental events lead to intrusions of memory representations. Secondly, it is postulated that disturbances in contextual binding (in which memories lack contextual details to bind them in time, place and person) lead to failures in correctly identifying the origin of these intrusions. This theory is supported by experimental evidence showing that people with a diagnosis of schizophrenia who have auditory hallucinations show poorer performance on tasks involving intentional inhibition (Waters, Badcock, Maybery, & Michie, 2003) and in combining contextual information to generate integrated memories for events (Waters, Maybery, Badcock, & Michie, 2004) than people with a schizophrenia diagnosis and no auditory hallucinations. However, of note, a third of the non-hallucinating group in these studies also showed the same pattern of difficulties with inhibition and contextual memory, suggesting that these difficulties alone are not able to explain the presence of auditory hallucinations. To date the findings regarding difficulties with inhibition and contextual memory have

only been tested in populations with a schizophrenia diagnosis, so further research is needed to explore whether they are also present in other clinical and nonclinical groups with auditory hallucinations.

2.4.5 Cognitive-behavioural models

Cognitive behavioural theories of psychotic symptoms hypothesise that psychotic experiences are rooted in anomalous experiences (e.g. heightened perception, racing thoughts, thoughts experienced as external (Garety, Kuipers, Fowler, Freeman, & Bebbington, 2001) and intrusions (Morrison, 2001) caused by cognitive and affective disturbances. These theories place importance on the role of appraisals of these experiences in the expression of frank psychotic symptoms. Negative schematic beliefs, reasoning biases, and emotional processes are hypothesised to contribute to threatening and external explanations of anomalous experiences and intrusions. In the case of auditory hallucinations, the appraisal that anomalous experiences or intrusions are from an external source leads to them being experienced as a hallucination (Garety et al., 2001; Morrison, 2001). A cognitive behavioural model of auditory hallucinations developed by Chadwick and Birchwood (1994) and updated by Birchwood, Meaden, Trower, Gilbert, and Plaistow (2000) also placed appraisals of auditory hallucinations centrally, postulating that beliefs about the power and omnipotence of voices (influenced by interpersonal schemata) were the main driving factor in distress. This theory of auditory hallucinations does not speculate as to the cause of the auditory hallucinations themselves, but instead focuses on cognitive, emotional and behavioural responses that lead to and maintain distress.

Cognitive behavioural models of auditory hallucinations have been beneficial in that they have provided a clear basis for developing psychological therapies for auditory hallucinations. The focus on beliefs and appraisals aligned psychological

therapies for psychosis with well-evidenced cognitive behavioural therapies for anxiety disorders and depression, which also place appraisals and beliefs centrally. This meant that psychological therapies for psychosis could be derived from already developed techniques and strategies. However, these theories have predominantly focused on psychological processes that maintain auditory hallucinations and related distress, and do not provide a comprehensive explanation of the cause of the experience of auditory hallucinations themselves.

2.4.6 Trauma and dissociation

Growing recognition of the prevalence of traumatic events in the life histories of people who experience auditory hallucinations has led to a burgeoning body of research and theory regarding trauma-related and dissociative processes that may be involved in auditory hallucinations. These theories are central to this thesis and as such will be described in detail in Chapters 3 and 4.

2.4.7 Limitations of current theoretical models of auditory hallucinations

Much of the research examining neurocognitive models of auditory hallucinations is based on experimental paradigms including, for example, source monitoring and verbal self-monitoring tasks (that require participants to make decisions regarding the source of self- or other-generated material), and auditory signal detection tasks (that require participants to detect auditory signals against background noise). These experimental tasks are likely to employ a range of cognitive functions, which limits inferences about the specific processes postulated to play a role. For example, it is possible that findings from these and other tasks might be accounted for by general cognitive impairments. The majority of studies in this area have also only included participants with diagnoses of schizophrenia spectrum

disorders, which may limit the generalisability of findings to auditory hallucinations that occur in other diagnostic groups or in nonclinical populations.

A general major limitation across current neurocognitive and psychological current of auditory hallucinations is also their failure to provide a comprehensive explanation of the diverse phenomenological aspects of auditory hallucinations. For example, models that depict auditory hallucinations as misattributed inner speech are a good phenomenological fit to auditory verbal hallucinations that characterised by content reflecting regulation of everyday activities (e.g. running commentaries) or that are commanding (Jones, 2010); however, they fail to account for the auditory quality of many auditory hallucinations (i.e. that auditory verbal hallucinations often have complex acoustic properties of pitch, timbre etc. that give the experience of someone else's voice; Cho & Wu, 2013). Similarly, these accounts are unable to explain nonverbal hallucinations that commonly co-occur with auditory verbal hallucinations. Conceptualisations of auditory hallucinations as unintentional intrusions of memory material are consistent with the fact that 39% of people report that their auditory hallucinations are replays of memories (McCarthy-Jones et al., 2014) and are better able to explain nonverbal auditory hallucinations, but less able to account for auditory verbal hallucinations that constitute a 'running commentary' of current events, or command hallucinations. Finally, the hypervigilance theory of auditory hallucinations is also only able to explain auditory hallucinations that occur in the presence of external auditory stimuli and that are experienced outside the head.

These limitations imply two possibilities. Firstly, it may be that we are yet to find the unifying mechanism involved in all auditory hallucinations. It has recently been suggested that 'predictive processing' models are more able to provide an overarching unified theory of auditory hallucinations (Wilkinson, 2014). In this model

conscious percept is not determined by incoming stimuli (memory intrusions, inner speech), but is determined by the brain's best hypothesis about what it is happening. This theory is more able to explain a diverse range of phenomenological aspects of auditory hallucinations because the perceived content and nature of the auditory hallucination is shaped by expectations, rather than by the incoming stimuli. Thus, an auditory hallucination can be perceived as having auditory qualities, because this is what the brain is predicting.

The second possibility is that different processes are involved in different types of auditory hallucinations. The possibility of subtypes of auditory hallucinations was examined using cluster analysis in a large phenomenology study, finding four main clusters of characteristics (McCarthy-Jones et al., 2014). The first cluster consisted of constant commanding and commenting auditory verbal hallucinations. The second cluster were described as 'own thought' auditory verbal hallucinations, characterised by first person voices, possibly considered to be one's own voices or thoughts. The third cluster was nonverbal hallucinations and the final cluster was 'replay' auditory verbal hallucinations that were identical to a memory of heard speech. The authors went on to argue that these clusters indicate distinct subtypes of auditory hallucinations that are caused by different mechanisms, including a hypervigilance subtype, an autobiographical memory subtype, and an inner speech subtype (McCarthy-Jones et al., 2014). This proposition is compelling in its ability to explain why no single theory has yet been able to account for all auditory hallucinations. It also holds promise in advancing research into the causes of auditory hallucinations by delineating these different subtypes and examining them as different phenomena. Despite the idea of mutually exclusive subtypes of auditory hallucinations being a conceptually attractive idea, most participants in the original

study experienced multiple subtypes, which suggests overlap between causal mechanisms involved.

2.3 The current status of treatments for auditory hallucinations

For many years treatment development for auditory hallucinations focused predominantly on uncovering and examining the efficacy of pharmacological interventions. This treatment approach is based on the dominant biological model that conceptualises auditory hallucinations as part of a cluster of experiences characteristic of schizophrenia and other psychotic disorders and caused by biological processes. These pharmacological treatments have therefore targeted a broad range of psychotic symptoms in people with a diagnosis of schizophrenia, with auditory hallucinations as one aspect of this. Evidence for these treatments has shown beneficial, but modest results (Samara, Nikolakopoulou, Salanti, & Leucht, 2018). Effect sizes across antipsychotic medications are generally in the small to medium range for psychotic symptoms and many have significant side-effects (Leucht et al., 2013). There does not appear to be any particular antipsychotic with a differentially superior impact on hallucinations specifically (Sommer et al., 2012).

Over the last twenty five years cognitive behavioural therapy for psychosis (CBTp) has been established as an evidence based adjunctive or alternative psychological treatment for psychotic symptoms. Clinical guidelines have recommended the widespread dissemination of this treatment (Kreyenbuhl, Buchanan, Dickerson, Dixon, & Schizophrenia Patient Outcomes Research Team, 2010; National Institute of Clinical Excellence, 2014). Cognitive behavioural therapy for psychosis was initially developed based on cognitive models of depression and anxiety disorders. Cognitive models posit that the way that we interpret events impacts on our emotions and behaviours, and that problematic interpretations can be maintained by

unhelpful behavioural responses and thinking biases. As previously outlined, cognitive behavioural models of psychosis emphasise that interpretations and responses to psychotic experiences drive distress and impairment, rather than the psychotic experiences themselves (Chadwick & Birchwood, 1994; Garety et al., 2001; Morrison, 2001). There have been a number of treatment manuals outlining approaches that aim to reduce distress and impairment by changing unhelpful interpretations, thinking biases, and problematic behavioural responses (Chadwick, Birchwood, & Trower, 1996; Fowler, Garety, & Kuipers, 1995; Kingdon & Turkington, 1994; Morrison, Renton, Dunn, Williams, & Bentall, 2003).

Despite being the current best evidenced psychological intervention for distressing psychotic experiences, CBTp only has small to moderate effects on psychotic symptom severity (Jauhar et al., 2014; Wykes, Steel, Everitt, & Tarrier, 2008), small effects on functioning (Laws, Darlington, Kondel, McKenna, & Jauhar, 2018), with one meta-analysis reporting no benefits for distress or quality of life when adjusting for possible publication bias (Laws et al., 2018).

Amidst a robust debate about the efficacy of CBTp (McKenna & Kingdon, 2014), important shortcomings with current evidence have been identified (Thomas, 2015). Firstly, CBTp has become a 'catch all' term for a broad range of therapy techniques that are generally delivered according to individualised formulations of symptoms and goals for therapy. Clinical trials of CBTp have usually included participants based on the presence of a specific diagnosis (schizophrenia or schizophrenia spectrum disorders). Since people meeting diagnostic criteria for schizophrenia spectrum disorders can present with significant symptom heterogeneity, this means that the goals and targets of therapy (and therefore the therapy techniques used) can differ widely between participants. Treatments included in these CBTp

trials may therefore include therapeutic approaches that target hallucinations, delusions, thought disorder, or negative symptoms, as well as other mood and anxiety related symptoms. This may impact on the evidence in two ways: firstly, it is difficult to disentangle which of the multifaceted components of CBTp are contributing to the effects seen and secondly, examining outcomes as a single group may obscure the effects of specific techniques that are particularly effective for specific symptoms. These issues are also confounded by the use of omnibus measures of symptom severity (for example using the Positive and Negative Syndrome Scale; Kay, Fiszbein, & Opler, 1987, rather than symptom specific measures). These broad outcome measures may lack sensitivity to capture treatment effects on specific symptoms targeted by CBTp (Birchwood & Trower, 2006).

Whilst CBTp remains a useful object of enquiry as a protocol for current best-practice psychological interventions that can be compared to other (e.g. pharmacological) treatments for psychosis, it appears that it is now also important to move beyond trials that consider CBTp a unitary therapeutic approach for people falling under particular diagnostic classifications. Instead, there has been a call for symptom-focused approaches that determine effects on specific symptoms. This has been a focus of recent CBT approaches to delusions (Freeman, 2011) and has been highlighted as a vital approach to improving psychological therapies for hallucinations (Thomas et al., 2014). In line with this proposal, recent meta-analyses have examined specific effects of CBTp approaches on hallucination outcomes, finding small to moderate effect sizes ($d =0.45$, $d = 0.44$; Naeem et al., 2016; van der Gaag, Valmaggia, & Smit, 2014). However, these meta-analyses are still based predominantly on trials of composite CBTp approaches, with heterogeneous client

symptom presentations, meaning that conclusions about the specific effects on hallucinations remain limited.

There are now a growing number of randomised controlled trials of psychological therapies that target auditory verbal hallucinations as a specific primary outcome. In the largest hallucination-specific trial to date, the COMMAND trial assessed the effects of cognitive therapy for command hallucinations on harmful compliance behaviours. When comparing the therapy group with a usual care control group this study found small to medium effects on compliance behaviour; however, there was no significant impact on voice-related distress (Birchwood et al., 2014). This study was large (n=197) and methodologically robust; however, the lack of an active control condition means that nonspecific therapy effects were not controlled for. Indeed, an Australian trial focused on command hallucinations using a similar therapy (CBT aimed at changing voice power beliefs, augmented with acceptance and commitment therapy strategies) did not find significant treatment effects when compared with an active befriending intervention control (Shawyer et al., 2012). In this study, both the CBT and the befriending groups improved, suggesting that nonspecific effects such as a therapeutic relationship and face-to-face contact time may account for positive changes. Another large trial of an innovative therapy using technology to create an avatar representing an individual's voices found large effects of the therapy on hallucination frequency and distress when compared to supportive counselling; however, these effects were not significant at 24-week follow up (The AVATAR trial; Craig et al., 2018). Again, the nonsignificant finding at follow up was due to improvements in the supportive counselling condition rather than loss of gains in the AVATAR therapy condition. This suggests that AVATAR therapy led to faster improvements that were maintained over time, but that supportive counselling also led

to similar gains over a longer time span. A smaller trial compared relating therapy, a therapy based on building up assertiveness in response to voices, to a treatment as usual control. This trial found large effects on hallucination-related distress, which were maintained at 20-week follow up (Hayward, Jones, Bogen-Johnston, Thomas, & Strauss, 2017). A guided self-help CBT intervention found large effects on the impact of auditory verbal hallucinations at the end of therapy when compared with a wait-list control group, but did not have a follow up assessment point (Hazell, Hayward, Cavanagh, Jones, & Strauss, 2018). Finally, the COMET trial examined the effects of competitive memory training, in which memories associated with positive self-esteem are retrieved and strengthened, compared with a treatment as usual control. There was no significant different on overall auditory hallucination severity post therapy; however medium effects were found for the reduction of negative appraisals of auditory hallucinations (van der Gaag, van Oosterhout, Daalman, Sommer, & Korrelboom, 2012). A recent systematic review explored the effects of hallucination-specific interventions and concluded that the results are promising, with a trend towards stronger effects than the more generic CBTp approaches (Lincoln & Peters, 2018).

Despite this promise, there are some limitations with the current evidence base for hallucination specific therapies. Many of the trials have been small pilot studies (Hayward et al., 2017; Hazell et al., 2018; van der Gaag et al., 2012) that are underpowered to draw firm conclusions regarding efficacy. The largest trial to date (Birchwood et al., 2014) did not have an active control condition, meaning that nonspecific effects were not controlled. The two trials that did use an active control condition did not find a significant difference in the effects of the therapy above those of supportive counselling or befriending at the longest follow up time point. There

remains uncertainty regarding the efficacy of therapies that specifically target auditory hallucinations and it is not yet clear whether these therapies show benefits beyond supportive counselling or befriending. There is a need to develop more effective therapies and for large, well-controlled trials to examine their efficacy.

2.3 Using a process-based approach to treat auditory hallucinations

Approaches to therapy that focus on specific psychological processes that are involved in distinct symptoms have been gaining momentum in the broader field of psychological therapies and may helpfully inform the development and trialling of new therapies for auditory hallucinations. Prominent researchers have highlighted an important shift that has occurred in psychological therapies - away from approaches delivering defined therapy protocols according to specific diagnostic categories, toward a transdiagnostic approach in which the focus is on targeting core psychological processes (Hofmann & Hayes, 2018). The culmination of this paradigm shift has been coined 'process-based CBT'. Process-based CBT is informed by theoretical and empirical evidence regarding psychological mechanisms involved in distress and is based on therapeutic techniques that have been evidenced to change these specific mechanisms. This focus on individual level mediators and moderators of change is in line with increasing emphasis on personalised or precision medicine in biomedical sciences.

The identification that there may be meaningful subtypes of auditory hallucinations that have distinct causal mechanisms (McCarthy-Jones et al., 2014) suggests that an approach that focuses on empirically supported psychological processes that are relevant on an individual level may be a fruitful approach for improving therapies for auditory hallucinations. Indeed, there has been a call for an increased focus on identifying subtypes of auditory hallucinations and developing

distinct treatments addressing specific implicated causal mechanisms (Smailes, Alderson-Day, Fernyhough, McCarthy-Jones, & Dodgson, 2015) and to use empirical knowledge to develop new treatments that target putative psychological processes involved in auditory hallucinations (Thomas et al., 2014).

Early work on symptom-specific psychological treatment approaches for auditory hallucinations was grounded in empirical research relating to causal mechanisms and thus explicitly highlighted external attribution biases as a treatment target (Bentall, Haddock, & Slade, 1994). More recently, however, treatments have largely focused on one psychological mechanism (postulated to be implicated in distress rather than as a causal mechanism per se): perceived power differentials in the person's relationship with their auditory verbal hallucination (Birchwood et al., 2000). Perhaps most notably, cognitive therapy for command hallucinations was derived from a cognitive model of auditory verbal hallucinations that highlights the importance of appraisals of malevolence and omnipotence (Birchwood et al., 2014). Cognitive therapy for command hallucinations specifically aims to challenge beliefs about the power of the auditory verbal hallucination to reduce the likelihood of the person complying with commands. As previously outlined, this intervention was found to reduce compliance behaviour. Importantly, this trial was also able to show that the effects of the treatment were mediated by the hypothesised mechanism of action – the perceived power of the voice, as measured by the voice power differential scale (VPD; Birchwood et al., 2004). Similarly, the AVATAR trial encourages an increased sense of mastery and control over the auditory verbal hallucinations through interactions with the avatar, with results showing that the therapy did reduce the perceived omnipotence of the auditory verbal hallucinations (Craig et al., 2018). Relating therapy for voices also focuses on increasing assertiveness in relating to the

auditory verbal hallucinations and has found promising effects on distress (Hayward et al., 2017).

There is growing understanding of other psychological mechanisms that may be implicated in the genesis and maintenance of auditory hallucinations, but surprisingly this has not yet translated into new psychological treatment approaches that target these mechanisms. In contrast, psychological treatments for delusions and paranoid thoughts are increasingly grounded in empirical research into postulated psychological mechanisms. Daniel Freeman and colleagues have advocated for an approach to treatment development for delusions based on an *interventionist–causal approach* (Kendler & Campbell, 2009), focusing on one putative causal mechanism at a time, showing that an intervention can change this mechanism and then examining the impact of this intervention on delusions (Freeman, 2011). For example, the role of worry in delusions has been explored through introducing a short worry intervention, ensuring that the intervention does indeed reduce the mechanism of interest (worry), and then testing the effect on delusions (Freeman et al., 2015). Through this process, not only has worry has been substantiated as a causal factor in delusions, but the worry intervention has also been demonstrated to be an effective treatment component. Using the interventionist–causal approach, treatment modules targeting worry, self-esteem, sleep, reasoning biases, and safety behaviours have all been shown to act on the mechanism of interest and to reduce paranoia. These treatment modules are now being trialled in a modular, individualised therapy approach (Freeman, Bradley, et al., 2016; Freeman, Waite, et al., 2016). Arguably, treatment development for delusions has been significantly improved by taking this approach. A recent review of studies that have used interventionist–causal tests to examine causal mechanisms involved in delusions and hallucinations highlighted that there are very

few studies that have used this paradigm to explore causal mechanisms involved in hallucinations, with the majority of work in this field having been focused on delusions (Brown, Waite, & Freeman, 2019).There is the possibility that an increased focus on causal mechanisms and tests of treatments that manipulate these mechanisms in an interventionist–causal paradigm may provide a much needed progression in therapies for auditory hallucinations.

2.4 Chapter summary

This chapter has provided some background context, noting that auditory hallucinations are relatively common across different psychiatric diagnoses and are often (but not always) associated with significant distress. There are a number of psychological theories attempting to explain the aetiology and maintenance of auditory hallucinations. None of these theories is able to explain the full range of phenomenological features of auditory hallucinations and it is likely that there are a number of psychological processes involved in auditory hallucinations that are of differing importance for each individual. Current best practice psychological therapies for auditory hallucinations have shown modest benefits and it has been suggested that psychological therapies can be improved by taking a symptom-focused approach that is based on targeting empirically derived psychological mechanisms. There are a handful of treatment studies that have taken a symptom-focused approach, but these studies have all targeted the same putative psychological mechanism – beliefs about power and omnipotence. Given growing evidence of other psychological mechanisms that may be involved, there is an opportunity to improve psychological therapies for auditory hallucinations by drawing on this literature to develop and test new interventions and strategies.

Chapter Three: Trauma, Adversity, and Auditory Hallucinations

3.1 Do trauma and adversity play a causal role in psychotic symptoms?

One candidate causal pathway that may be fruitful to examine in informing psychological therapies for auditory hallucinations using a process-based approach is that of trauma and adversity. Traumatic and adverse life events in childhood, including physical, sexual, and emotional abuse, neglect, and interpersonal victimisation, are common in the life histories of people who experience psychosis. Up to 85% of people with schizophrenia spectrum disorders report emotional, physical, or sexual abuse, or emotional or physical neglect (Larsson et al., 2013).

In the last two decades there has been mounting evidence that exposure to trauma and adversity may represent a significant risk factor in the development of psychotic symptoms (Bendall, Jackson, & Hulbert, 2010; Bendall, Jackson, Hulbert, & McGorry, 2008; Read & Bentall, 2012; Read, Perry, Moskowitz, & Connolly, 2001). There is now a large body of robust evidence that indicates that trauma has a causal role in the development of psychosis.

The field of epidemiology has developed several criteria that need to be established to infer a relationship between an environmental exposure and a specific health outcome. Most notably, the 'Bradford Hill' criteria (Hill, 1965) have been widely used to evaluate the likelihood of causal relationships in the field of medicine. Rather than considering these criteria to be rules that must be fulfilled for a relationship to be concluded to be causal, Hill conceptualised them as a means of examining whether a causal relationship between an environmental variable and a particular health outcome is a reasonable inference. Hill outlined nine criteria: strength, consistency, dose-response, temporality, specificity, experimental evidence,

analogy, plausibility, and coherence. These criteria can thus be used as a framework to evaluate the likelihood of a causal relationship between trauma and psychosis.

3.1.1 Strength of the relationship

Firstly, the strength of an association between two variables is important, with strong associations between variables more likely to be indicative of a causal relationship than weak associations. Data regarding the strength of the association between trauma and psychosis has been synthesised in a meta-analysis of 41 articles, including patient-control, prospective, and cross-sectional cohort studies (Varese et al., 2012). This meta-analysis included studies examining the relationship of childhood sexual, physical, and emotional abuse, childhood physical and emotional neglect, bullying, and parental death (before age 18) with psychotic disorders or psychotic symptoms. The meta-analysis found that childhood adversity and trauma substantially increase the risk of psychosis, with an odds ratio of 2.78 (95% CI 2.34-3.88). The estimated population attributable risk was 33% (95% CI 16-47%), meaning that if childhood trauma and adversity were eradicated, there would be an estimated 33% less cases of psychosis (Varese et al., 2012). Matheson, Shepherd, Pinchbeck, Laurens, and Carr (2013) also meta-analysed case-control, cohort, and cross-sectional findings, specifically looking at the relationship between childhood adversity (including sexual abuse, physical abuse and neglect) and schizophrenia, also finding that childhood trauma increased the risk of schizophrenia more than threefold (OR 3.6). Since these important meta-analyses, several reviews have reported similar results, reporting odds ratios in the range of two to four (as reviewed by Morgan & Gayer-Anderson, 2016). The strength of the association makes childhood trauma and adversity one of the most robust risk environmental risk factors for psychosis (Belbasis et al., 2018). However, despite a strong association between trauma and

adversity, this alone does not necessarily imply a causal relationship. Studies included

in these meta-analyses have been predominantly cross-sectional, which means that

reverse causality (i.e. that psychosis precedes trauma) or confounding variables in the

relationship (for example, economic deprivation, genetic factors, or urbanicity) cannot

be ruled out.

3.1.2 Consistency of the relationship

If a variable is causing a particular outcome then one would expect consistent findings

with regard to their relationship across different studies, regardless of the context or

the methods used. Findings regarding the link between trauma and psychosis have

also been largely consistent. Within Varese's meta-analysis only one of the 41 studies

included did not find a relationship between childhood trauma and psychosis

(Furukawa et al., 1998), which specifically looked at the role of the death of a parent

in schizophrenia. Notably, the meta-analysis included studies using different

methodologies (case-control, cross-sectional, and prospective cohort studies) and

across different populations (nonclinical and clinical). As noted above, reviews

published since Varese's meta-analysis have also reported consistent results, finding

odds ratios in the range of two to four (Morgan & Gayer-Anderson, 2016). The

relationship between childhood trauma and psychosis has also been found to persist

when potential confounding variables, such as psychiatric comorbidities, genetic risk,

and cannabis use, are controlled for (Arseneault et al., 2011; Heins et al., 2011; Lecei

et al., 2018).

3.1.3 A dose-response relationship

A biological gradient, or 'dose–response' relationship is also considered to be

particularly indicative of a causal relationship. In a dose response relationship, the risk

or severity of the outcome is found to increase as the dose of the putative causal

variable is increased. The dose–response effect between childhood trauma and psychosis has not been systematically synthesised in a meta-analysis due to heterogeneity in the way this effect has been measured in different studies. However, Varese et al. (2012) report that nine out of 10 studies that assessed for it did find a dose–response relationship. Since this time, multiple studies have reported a dose–response relationship between childhood trauma and psychosis outcomes (Trauelsen et al., 2015; Longden, Sampson, & Read, 2015; Croft, Heron, Teufel, & et al., 2018; Kelleher et al., 2013; Morgan et al., 2014; van Dam et al., 2015; van Nierop et al., 2015). Again, a dose response relationship increases the likelihood of a causal relationship between two variables, but is not sufficient evidence to draw this conclusion, since association that is explained by confounding variables may still have a dose-response relationship. For example, if cannabis use explained the relationship between trauma and psychosis, then we would still expect to see a dose response relationship, as higher levels of trauma may lead to more cannabis use, thus leading to higher risk of psychosis.

3.1.4 Temporality in the relationship

A significant weakness in the literature to date has been that most studies have been cross-sectional patient-control or cohort studies. While these studies can provide indications regarding the strength and consistency of the relationship between trauma and psychosis, they are limited at establishing temporal relationships. For a variable to play a causal role in an outcome, exposure to that variable necessarily has to occur before the outcome of interest. There are now several very robust prospective studies that provide compelling evidence of temporality in the relationship between trauma and psychosis. Aresenault et al. (2011) used longitudinal and prospective measures of trauma during childhood (assessing 2,232 children at age five, seven, 10, and 12) and

found maltreatment and bullying (but not accidents) to predict psychotic symptoms at age 12. However, psychotic symptoms were only assessed at age 12, limiting conclusions about the temporal ordering of the traumatic experiences and psychotic symptoms. In addition, this study did not follow up participants beyond the age of 12, which restricts the inferences that can be made regarding psychotic symptoms that persist into or develop in late adolescence or adulthood.

In a prospective cohort study of 1,112 adolescents who were assessed at three time points over a one year period, Kelleher et al. (2013) found that physical assault and bullying experiences had a bidirectional association with psychotic experiences. To specifically assess the hypothesis that trauma plays a causal role in psychotic symptoms the authors also explored whether traumatic experiences predicted new incidences of psychotic experiences (i.e. a causal pathway in the direction of trauma leading to psychotic symptoms rather than vice versa). This analysis confirmed that trauma predicted new incidences of psychotic experiences. Importantly, it was found that when exposure to trauma ceased, psychotic experiences decreased significantly. These findings strengthen causal inferences regarding the relationship between trauma and psychotic symptoms considerably; however, it should be noted that the study only measured physical assault and bullying and did not assess other types of traumatic events that have been associated with psychotic symptoms (e.g. sexual abuse and emotional neglect). This study also only followed participants over the space of a year, which limits conclusions about the relationship between childhood trauma and psychotic symptoms that endure into adolescence and adulthood. In the largest and most robust study to date, Croft et al. (2018) conducted an analysis of data from the ALSPAC longitudinal cohort study (Avon Longitudinal Study of parents and Children, n = 4433) and found that exposure to any trauma from age 0 to 17 years

increased the odds of psychotic experiences at 18 years (OR = 2.91). The study examined six different types of traumatic event (covering inter-personal violence and neglect) and used a semi-structured interview to assess for psychotic experiences. This study undertook sensitivity analyses to control for reverse causality (i.e. that early psychotic experiences increase the risk of trauma); the association between trauma and psychotic experiences was substantively the same when participants reporting psychotic experiences at age 12 were excluded (ensuring that the psychotic experiences analysed did not precede the traumatic events). Analyses in this study also adjusted for a comprehensive range of confounding variables, including genetic risk for psychiatric disorders, family characteristics, socio-economic adversity, and markers of childhood development. A further strength of this study is that participants were followed until 18 years old. Psychotic disorders most commonly have their onset in late adolescence and early adulthood, so it is important to follow up cohorts into this age range. Future studies need to examine whether the relationship between early trauma and psychotic symptoms endures beyond 18 years of age.

3.1.5 Specificity of the relationship

Childhood trauma and adversity show a relationship with a range of psychiatric diagnostic outcomes. It is therefore possible that the relationship seen between trauma and psychosis is nonspecific, that is, trauma has general impacts on a variety of bio-psycho-social processes, related to multiple diagnostic outcomes. Indeed, studies that have examined the effects of broadly defined childhood trauma and adversity have found that they are associated with an increased risk for multiple disorders. In a meta-analysis comparing the association of childhood trauma with a variety of psychiatric diagnoses, Matheson et al. (2013) found that there was no difference in the magnitude of the relationship found for schizophrenia than that

found for affective psychosis, depression and personality disorders. Schizophrenia did show a stronger relationship with childhood trauma than that found for anxiety disorders, but a weaker relationship than that for PTSD and dissociative disorders. The authors concluded that rather than increasing risk for a specific disorder, childhood trauma increases the risk of stress-related disorders through neurobiological changes related to the regulation of stress responses (particularly the hypothalamic-pituitary-adrenal axis). In a large cross-sectional study of the general population (NEMESIS-2), van Nierop et al. (2015) similarly found largely comparable associations between childhood trauma and depression, mania, anxiety, and psychosis. This study found that individuals who had experienced childhood trauma were more likely to have a combination of multiple symptom domains, compared to those without a childhood trauma history. These findings are again consistent with childhood trauma leading to multiple symptoms, including psychosis. Gibson et al. (2016) reviewed relevant literature in the area and concluded that the specificity of a relationship between trauma and psychosis in comparison to other psychiatric diagnoses is unclear but assert that this does not undermine the robust association between trauma and psychosis. Notably, the relationship between trauma and psychosis has been shown to persist even when comorbidity is controlled for (Varese et al., 2012), suggesting that the relationship is not solely due to the presence of other psychiatric symptoms, but shows a specific relationship above and beyond this. Indeed, Gibson et al. (2016) highlight the importance of examining and understanding specific mechanisms that explain the link between trauma and psychosis, once all comorbid symptomatology is accounted for.

Another aspect of specificity in the relationship between trauma and psychosis that is important is whether there is specificity in the effects of specific types of

trauma with specific symptoms of psychosis. Meta-analytic evidence has suggested that the association between childhood trauma and psychosis is present regardless of trauma type. For example, Varese et al.'s (2012) meta-analysis found no significant difference between the odds ratios for sexual abuse, physical abuse, emotional abuse, bullying, and neglect. Other robust studies since this time have also suggested that relationships between trauma and psychosis do not differ significantly across trauma types, instead finding the number and severity of trauma exposures to be more important than trauma type (Croft et al., 2018). However, some studies have suggested that particular types of traumatic events may have stronger relationships with psychosis. Fisher et al (2010) examined the impact of various aspects of childhood experiences of care and abuse in a first episode psychosis sample and a matched control. After adjusting for other types of adversity and demographic confounders, the only type of adversity to show a relationship with psychosis was maternal physical abuse. Other studies have found that traumatic events characterised by intention to harm show specific relationships with psychosis (Arseneault et al., 2011; van Nierop et al., 2015).

Generally, associations between trauma and the positive symptoms of psychosis have been much more robust (Ajnakina et al., 2016). Read, van Os, Morrison, and Ross (2005) reviewed 26 studies examining the link between childhood trauma and hallucinations or delusions and found that there was particular evidence for a role of sexual abuse in hallucinations. This specific relationship between childhood sexual abuse and auditory hallucinations has also been demonstrated in two large, robust studies (Bentall, Wickham, Shevlin, & Varese, 2012; Sitko, Bentall, Shevlin, O'Sullivan, & Sellwood, 2014). These studies also found a specific relationship between parental separation or neglect and paranoia (Bentall et al., 2012;

Sitko et al., 2014). More recently, Hardy et al. (2016) found auditory hallucinations to be associated with sexual abuse (OR = 2.3), but not to be associated with physical or emotional abuse or non victimisation trauma, and childhood emotional abuse, but not physical abuse to be associated with persecutory (OR = 2.21) and referential delusions (OR = 2.43).

Because auditory hallucinations are the particular focus of this thesis, the specific association between traumatic and adverse events and auditory hallucinations will be considered in detail in Section 3.2.

3.1.6 Experimental evidence

Hill (1965) outlined that evidence drawn from experimental manipulation, in which disease risk declines following an intervention or cessation of exposure, may lead to the strongest support for causal inference. There have been no experimental studies examining the effects of interventions that reduce or stop traumatic events; however, there is now compelling evidence from one longitudinal cohort study that if trauma exposure ceases, the risk of psychotic experiences decreases (Kelleher et al., 2013). A lack of experimental evidence is understandable given the obvious ethical issues with controlled manipulation of trauma exposure.

3.1.7 Analogy

Hill (1965) also outlined that when there is strong evidence of a causal relationship between a particular variable and specific health outcomes, then it is more likely that a similar variable will cause an analogous health outcome. In the case of trauma and psychosis, there are several analogies that can be drawn. Firstly, there is compelling evidence for other environmental factors playing a causal role in psychosis, for example urbanicity (Vassos, Pedersen, Murray, Collier, & Lewis, 2012). Likewise, there is growing evidence that childhood trauma plays a causal role

in a variety of psychiatric diagnostic outcomes (van Nierop et al., 2015). Perhaps the most robust relationship that has been identified is that between childhood trauma and PTSD (Widom, 1999). The fact that trauma can lead to PTSD, which has symptom overlap with psychosis, is perhaps the strongest analogy strengthening the case for the role of trauma in psychosis.

3.1.8 Plausibility and coherence

The plausibility and coherence of causal relationships relates to whether there are plausible and coherent accounts regarding the mechanisms through which a variable may cause a particular outcome. There is a growing literature relating to potential causal mechanisms involved in the trauma-psychosis relationship, with several candidate mechanisms that plausibly mediate the trauma-psychosis association. This important area is discussed in detail in section 3.3.

Overall it can be concluded that there is a strong argument for traumatic events playing a causal role in psychosis. Research over the last three decades has shown strong, consistent, dose response relationships between childhood trauma and psychotic symptoms. Childhood trauma appears to precede psychotic symptoms and this effect reduces when trauma ceases. However, it should be noted that the majority of evidence thus far has been cross-sectional or has involved longitudinal studies that only cover a short time frame. Longitudinal evidence that early traumatic events predict persistent psychotic symptoms in adulthood will further strengthen causal inferences. A body of evidence has also begun to explore plausible mechanisms that might mediate a causal relationship between trauma and psychosis. Mechanisms specifically implicated in the trauma- auditory hallucination relationship are explored in Section 3.3.

3.2 The specific relationship between trauma and auditory hallucinations

Much of the literature reviewed so far relates to the role of trauma in psychosis and psychotic symptoms in general. Since this thesis takes a more symptom-specific approach, it is important to understand the literature relating specifically to the relationship between trauma and auditory hallucinations.

The work of Romme and Escher, founders of the *Hearing Voices Network*, transformed understanding of auditory hallucinations from un understandable and meaningless symptoms, to seeing them as inherently meaningful experiences that are commonly related to stressful or traumatic life events (Corstens, Longden, McCarthy-Jones, Waddingham, & Thomas, 2014). This followed their early research that found that 70% of people with auditory hallucinations reported that the onset of these experiences followed a traumatic or emotional life event (Romme & Escher, 1989). Since this pioneering work, the role of traumatic life events in auditory hallucinations has been explored using a variety of research approaches.

Read et al.'s (2005) review summarised all of the research prior to 2005 that had examined the relationship between childhood trauma and hallucinations. This review found evidence for a relationship between childhood abuse and hallucinations, proposing that there is a particular link between sexual abuse and hallucinations. Many of the studies included in this review were noted to have methodological weaknesses, such as relying on chart reviews to examine the presence of trauma (rather than using validated measures) and many having small sample sizes.

Since this time, there have been several more robust studies that have examined the specific relationship between childhood trauma and auditory hallucinations. Some of this research has found a link between multiple trauma types and auditory hallucinations. For example, Berg (2015) assessed 454 people with a

diagnosis of a psychotic disorder and found that sexual abuse, physical abuse, physical neglect, and emotional abuse were all related to current hallucinations. In another study, Daalman et al. (2012) compared a group of people with auditory verbal hallucinations and psychotic disorders (*n*= 100), with people with auditory verbal hallucinations and no psychiatric diagnosis (*n*= 127), and a control group with no psychiatric diagnosis and no auditory verbal hallucinations (*n*=124). They found that both of the groups with hallucinations reported significantly more sexual and emotional abuse than the control group. There was no difference between the two groups with hallucinations, suggesting that sexual and emotional abuse are related to the presence of hallucinations specifically, rather than to psychotic disorders more generally.

There has also been a body of research that has specifically linked sexual abuse experiences with auditory hallucinations. Sexual abuse experiences are prevalent in groups with auditory hallucinations. McCarthy-Jones (2011) reviewed studies that had examined the prevalence of childhood sexual abuse in people with auditory hallucinations, finding a combined weighted mean prevalence of 36%. In studies examining the prevalence of childhood trauma in nonpsychiatric populations with auditory hallucinations there was a weighted mean prevalence of 22%. Several large population studies have found a specific link between childhood sexual abuse and hallucinations. Shevlin, Dorahy, and Adamson (2007) examined the relationship between childhood trauma and hallucinations in the National Comorbidity Survey and found that only rape and molestation were significantly associated with auditory hallucinations. Similarly, Bentall (2012) and Sitko (2014) reported that rape and molestation were specifically related to reports of hallucinations in large population surveys. The odds ratio of experiencing hallucinations after rape and molestation was

found to be 8.9 (CI = 1.86-42.44) once comorbidities were controlled for (Bentall et al., 2012). In psychiatric populations, the specific relationship between sexual abuse and auditory hallucinations has also been apparent. As outlined in Section 3.1, Hardy et al. (2016) found auditory hallucinations to be associated with sexual abuse (OR = 2.3), but not to be associated with physical or emotional abuse or non victimisation trauma). Sheffield, Williams, Blackford, and Heckers (2013) found that people with psychotic disorders with a history of auditory hallucinations reported significantly more sexual, emotional and physical abuse than patients without a history of auditory hallucinations; however, when sexual abuse was controlled for, the relationship was no longer significant for emotional and physical abuse, again suggesting a specific relationship between childhood sexual abuse and hallucinations.

This literature suggests that trauma may play a specific causal role in auditory hallucinations. There is evidence for a general link between trauma and auditory hallucinations, and also indication that sexual abuse in particular may be important in this relationship. However, although studies carried out since 2005 have used more robust measures of trauma exposure and have generally had larger sample sizes, these studies are all cross-sectional, relying on retrospective reports of trauma-exposure and only demonstrate association, rather than causation. The longitudinal studies described in Section 3.1.4 (Arseneault et al., 2011; Croft et al., 2018) did not separately assess hallucinatory experiences, so specific conclusions regarding auditory hallucinations cannot be made. Interestingly, Kelleher et al.'s (2013) longitudinal study used a single item ("Have you ever heard voices or sounds that no one else can hear?") to assess for psychotic experiences. This item has been found to detect both hallucinations and delusions in adolescent populations and was therefore used as a general assessment of psychotic experiences; however, the emphasis on

auditory hallucinations perhaps suggests that there is a temporal relationship between traumatic events and auditory hallucinations. The temporal relationship between trauma and auditory hallucinations needs to be explored in longitudinal studies that specifically assess auditory hallucinations.

3.3 Psychological mechanisms involved in the trauma-auditory hallucination relationship

Research has gone a long way towards establishing that traumatic events play a causal role in auditory hallucinations. Understanding the specific mechanisms involved in the relationship between trauma and auditory hallucinations is now important to advance inferences of causality and to develop interventions that can ameliorate the impact of traumatic events. A focus on prevention of traumatic events and adversity in childhood is important; however, when people do experience significant trauma and adversity it is also crucial that we have effective interventions for the array of negative outcomes that can be related to these experiences. A number of potential mechanisms involved in the specific relationship between traumatic events and auditory hallucinations have been outlined at different levels of explanation (e.g. at the level of brain structures and brain chemistry); however, this review will focus on mechanisms at a psychological level of explanation, since this is most informative for psychological treatment development. Psychological theory and research have pointed towards three main groups of psychological mechanisms that may play a role: affective disturbance and dysregulation, negative schematic beliefs, and posttraumatic stress symptoms and sequelae (Williams et al., 2018).

3.3.1 Affective disturbance and dysregulation

Psychological models of psychosis have conceptualised affective processes to be central to the development of psychotic symptoms, with shifts in affect contributing to

the occurrence of anomalous experiences, as well as to negative appraisals of these experiences (Garety et al., 2001). It has been suggested that people who experience psychosis are more sensitive to environmental stressors, showing heightened affective responses to these triggering events (Inez Myin-Germeys & van Os, 2007). This increased sensitivity to stress may be one explanation for the relationship between traumatic events and psychosis. Read et al. proposed the *traumagenic neurodevelopmental model of psychosis* (Read, Fosse, Moskowitz, & Perry, 2014; Read et al., 2001) in which vulnerability to psychosis is caused by heightened sensitivity to stress that occurs due to neurodevelopmental changes in the brain following traumatic events. This theory was based on evidence that people with psychotic disorders show many of the same neuroanatomical and neurochemical differences as traumatised populations. These changes include over activity of the hypothalamic-adrenal-pituitary (HPA) axis, dopamine, serotonin and norepinephrine abnormalities and structural differences in the hippocampus, and frontal lobes (Read et al., 2014). Studies using the experience sampling method (ESM, also referred to as ecological momentary assessment, or EMA), in which data is gathered on repeated occasions in the context of daily life, have provided support of the role of stress sensitivity in the relationship between traumatic events and psychosis. An ESM study of 50 people with psychosis found that those who had experienced childhood trauma showed heightened emotional and psychotic responses to stressful events in daily life (Lardinois, Lataster, Mengelers, Van Os, & Myin-Germeys, 2011). This study used a composite of seven items to assess psychotic symptoms, but none of these items related to auditory hallucinations (one item related to visual hallucinations and the remainder related to paranoia and passivity experiences). A number of studies have also found that difficulties with regulating mood mediate the relationship between

trauma and psychosis (Williams et al., 2018). Much of this literature has also focused on psychosis as a composite outcome and has not provided data regarding the specific mediating role of affective dysregulation in the relationship between trauma and hallucinations. However, a study by Marwaha, Broome, Bebbington, Kuipers, and Freeman (2013) used data from the 2000 and 2007 UK national surveys of psychiatric morbidity and showed that mood instability mediated a quarter of the total association between childhood sexual abuse and auditory hallucinations. This study used a large sample and employed robust methods of mediation analysis. The idea of an affective pathway between trauma and psychotic symptoms has also been supported by a recent study using the novel network approach. Using data from 552 people diagnosed with a psychotic disorder, Isvoranu et al. (2017) modelled connections between childhood trauma and positive and negative symptoms of psychosis. The results showed that childhood trauma and positive and negative symptoms of psychosis were connected through symptoms of general psychopathology. In particular, childhood trauma was only linked to hallucinations through anxiety symptoms.

Attachment theory has outlined that mental representations of the self in relation to others, developed through early interactions with primary care givers are a key part of emotion regulation (Bowlby, 1973). These mental representations, or 'internal working models', guide attention, interpretation and predictions about interpersonal interactions. Berry and Bucci (2016) have proposed a *cognitive attachment model of voice-hearing,* which suggests that disorganised attachment (a pattern of attachment that involves confused and disoriented responses when seeking care) plays a role in the development of auditory hallucinations through increased vulnerability to dissociated self-states and trauma-related and self-critical thoughts. This model also hypothesises a role for insecure attachment styles in maladaptive

coping and appraisals of auditory hallucinations, which contribute to levels of distress. There is evidence that attachment styles do mediate the relationship between traumatic events and psychosis (Williams et al., 2018); however, much of this research is focused on aggregate psychotic symptoms, rather than auditory hallucinations alone. Studies that have explored the relationship between attachment styles and specific psychotic symptoms have found associations with paranoia, but not with hallucinations (Pearce et al., 2017; Wickham, Sitko, & Bentall, 2015). Further evidence is needed to elucidate the specific relationship between disorganised attachment, dissociation, and auditory hallucinations.

3.3.2 Negative schematic beliefs

Negative schematic beliefs are implicated in cognitive behavioural models of psychosis, with a suggestion that these negative beliefs about the self, world, and others shape anomalous experiences and contribute to distressing appraisals of these experiences (Garety et al., 2001). Negative schematic beliefs have also been implicated in auditory hallucinations specifically. Social schema (particularly those relating to one's social rank) are important in determining beliefs about the power and omnipotence of auditory hallucinations, which contribute to distress and compliance with commands (Birchwood et al., 2000; Paulik, 2012; Thomas, Farhall, & Shawyer, 2013). Negative schematic beliefs have also been proposed to contribute directly to negative auditory verbal hallucination content (Beck & Rector, 2003).

Cognitive behavioural models that have specifically aimed to explain the relationship between traumatic events and hallucinations have highlighted a potential role of posttraumatic negative schematic beliefs in shaping hallucination content and appraisals of hallucinations (Hardy, 2017; Morrison, Frame, & Larkin, 2003). Despite this, there is only limited research in support of this proposal. Negative beliefs about

the self and others have been found to mediate the relationship between trauma and hallucination proneness in a nonclinical sample (Gracie et al., 2007) and to predict hallucinatory experiences following a physical assault (Geddes, Ehlers, & Freeman, 2016). However, the majority of research exploring the role of negative schematic beliefs in the development of psychotic experiences has found a specific relationship with paranoia, rather than with auditory hallucinations (Peach, Alvarez-Jimenez, Cropper, Sun, & Bendall, 2018; Williams et al., 2018).

3.3.3 Posttraumatic sequelae

Dissociation can be defined as a disruption in the normal integration of psychological functions, such as memory, identity, consciousness, and perception (Spiegel, Loewenstein, Lewis-Fernandez & Sar, 2011). There is a strong relationship between traumatic events and dissociation in both clinical and nonclinical samples (Kluemper & Dalenberg, 2014) and dissociation has been considered to be a defensive response to overwhelming affect experienced during traumatic events (van der Hart, Nijenhuis, Steele, & Brown, 2004). Meta-analytic evidence has shown a large and significant relationship between dissociation and auditory hallucinations (Pilton, Varese, Berry, & Bucci, 2015). It has been proposed that auditory hallucinations are a trauma-induced dissociative experience caused by a failure to integrate aspects of the traumatic experience into the context of the self (Longden, Madill, & Waterman, 2012; Moskowitz & Corstens, 2007). Indeed, in recognition of dissociation as a common posttraumatic sequelae, the DSM 5 has included a dissociative subtype of posttraumatic stress disorder (American Psychiatric Association, 2013). These proposals are supported by evidence that dissociation mediates the relationship between adverse life experiences and auditory hallucinations (Perona-Garcelán et al., 2011; Perona-Garcelán et al., 2012; Varese, Barkus, &

Bentall, 2012). Evidence in this area has also moved beyond cross-sectional studies and shown that dissociation is a momentary predictor of auditory hallucinations in daily life (using EMA methodology; Varese, Udachina, Myin-Germeys, Oorschot, & Bentall, 2011).

The core symptoms of posttraumatic stress disorder (PTSD) have also been implicated in the relationship between traumatic events and auditory hallucinations. As the central focus of this thesis, literature relating to this association is explored in more depth in Chapter 4.

3.3.4 Critique of research relating to the psychological mechanisms involved in the trauma-auditory hallucination relationship

A significant limitation of the current literature relating to psychological mechanisms involved in the relationship between trauma and auditory hallucinations is that the majority of theories and studies have focused on psychological mechanisms that play a role in the relationship between traumatic events and psychosis in general, rather than exploring mechanisms involved in specific psychotic symptoms. There is limited evidence and theory relating specifically to trauma-related psychological mechanisms involved in auditory hallucinations.

Of note, there is also little research regarding the role of trauma in neurocognitive processes that have long been implicated in auditory hallucinations (e.g. self- and source monitoring difficulties). It may be that drawing on literature regarding well established mechanisms involved in auditory hallucinations can improve our understanding of the role that trauma plays in the genesis of auditory hallucinations. For example, it is not clear whether traumatic life experiences predispose people to difficulties in self- and source monitoring and this mediates the relationship between traumatic events and auditory hallucinations.

A second major limitation of the literature that is available in this area is that the majority of studies conducted have been cross-sectional and have therefore examined the relationship between an aggregate measure of the putative mechanism and aggregate measure of psychotic symptoms at one time point. When examining the role of psychological mechanisms in the genesis of auditory hallucinations, psychological theory would suggest a more dynamic, moment-to-moment relationship (i.e. that the mechanism of interest is associated with momentary occurrences of auditory hallucinations). Cross-sectional studies are not able to explore this dynamic relationship. Research in this area has, however, begun to utilise new technologies to capture the momentary role of trauma-related psychological mechanisms. Notably, Varese et al. (2011) used EMA to explore the role of dissociation in predicting the occurrence of auditory hallucinations in daily life. The EMA method and its potential in understanding the role of posttraumatic psychological mechanisms in auditory hallucinations will be described in more detail in Chapter Seven of this thesis.

3.4 Chapter summary

This chapter has posited that there is sufficient evidence to suggest that traumatic life events play a causal role in the development of psychotic symptoms, including auditory hallucinations. Many of the Bradford Hill criteria have been met, with evidence suggesting strong consistent relationships between trauma and psychotic symptoms that occur in a dose response fashion, and in the temporal order expected. There is now a need to understand the mechanisms through which trauma leads to auditory hallucinations. At a psychological level of understanding, there is growing evidence for three main 'families' of psychological mechanisms as mediators in the relationship between trauma and auditory hallucinations: affective disturbance and dysregulation, negative schematic beliefs, and posttraumatic sequelae. Research

has been limited by a focus on psychotic symptoms in general, rather than a symptom specific focus on auditory hallucinations. Studies have also been predominantly cross-sectional and are therefore limited in explicating the moment-to-moment relationships that psychological theories would predict, and in making causal inferences.

The role of PTSD symptoms and trauma memory processing are the main focus of this thesis and will therefore be explored in depth in Chapter Four.

Chapter Four: The Specific Relationship Between Posttraumatic Stress Disorder and Auditory Hallucinations

4.1 Posttraumatic stress disorder and auditory hallucinations: diagnostic, symptom, and phenomenological overlap

Posttraumatic stress disorder (PTSD) is generally considered to be the 'hallmark' psychological disorder caused by traumatic events. By definition, a diagnosis of PTSD requires that someone has been exposed to a potentially traumatic event. The diagnostic classification of PTSD underwent significant changes in the most recent revisions of the DSM-5 (American Psychiatric Association, 2013) and the International Classification of Diseases 11th edition (ICD-11; World Health Organisation, 2018). The DSM-5 stipulates that an individual needs to have been directly or indirectly exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence. Symptoms are then required across four categories: intrusions, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity. The ICD-11 aims to increase the specificity of a PTSD diagnosis and therefore requires the presence of six symptoms considered to be core defining features of PTSD: dissociative flashbacks, nightmares, hypervigilance, exaggerated startle response, avoidance of external reminders, and avoidance of thoughts and feelings associated with the traumatic event. Both classification systems require the symptoms to have been present for over a month. The lifetime prevalence rate of PTSD in the general population in Australia is 7.2% (McEvoy, Grove, & Slade, 2011).

There are high rates of comorbidity between PTSD and psychotic disorders. There was a high level of heterogeneity in prevalence figures for PTSD in populations with psychotic disorders in a systematic review of 34 studies, with prevalence

estimates ranging between 0 and 57%, but most being in the range of 20 to 30%

(Seow et al., 2016). This review identified that included studies used heterogeneous

samples and differing methods of assessing PTSD symptoms (with studies using self-

report measures finding the highest rates). The most robust study in this area found a

prevalence rate of 16% in a sample of 2608 people with a psychotic disorder who

were screened using the Trauma Screening Questionnaire and had PTSD diagnosis

verified PTSD using the Clinician Administered PTSD scale (considered the 'gold

standard' clinical interview for a DSM diagnosis of PTSD; de Bont et al., 2015).

Despite heterogeneity among studies, the literature does indicate elevated rates of

PTSD in populations with psychotic disorders.

People with a PTSD diagnosis also show relatively high levels of comorbid

psychotic symptoms, particularly auditory hallucinations. Again, estimates of the

prevalence of auditory hallucinations have differed depending on the population

studied and methods of assessment used. Anketell et al. (2010) assessed 40 people

with chronic PTSD (a mixed civilian and military sample) using the hallucinations

subscale of the Positive and Negative Syndrome Scale (Kay et al., 1987) and found

that 50% of this group reported auditory verbal hallucinations. In contrast, Sareen,

Cox, Goodwin, and Asmundson (2005) examined Composite International Diagnostic

Interview (CIDI) data from the National Comorbidity Survey and found that questions

relating to auditory hallucinations were only endorsed by 2.8 to 5.1% of people

meeting criteria for PTSD (depending on the specific CIDI item). A retrospective

cohort study that examined psychiatric records from 220 consecutive patients at a

traumatic stress clinic for refugees found that 28% of this group reported experiencing

auditory hallucinations (Nygaard, Sonne, & Carlsson, 2017). Again, despite some

heterogeneity in prevalence rates between studies in this area, it is clear that many

people who meet diagnostic criteria for PTSD do also experience auditory hallucinations. Auditory hallucinations that occur in people with PTSD had previously been conceptualised to be different from those seen in people with psychosis, being ego syntonic and dissociative in nature ('pseudo hallucinations'), in contrast to those seen in psychotic disorders being ego dystonic and experienced as externally generated ('true hallucinations'; Brewin & Patel, 2010). However, there is a growing body of evidence that does not support this proposition, but instead indicates that auditory hallucinations in PTSD and psychotic disorders share a qualitatively similar phenomenology, suggesting that there is not a clear differentiation (McCarthy-Jones & Longden, 2015).

There is also very robust evidence that a PTSD diagnosis presents a significant risk factor for the subsequent development of a schizophrenia spectrum disorder. In a prospective cohort study of the entire Danish population over two decades, Okkels, Trabjerg, Arendt, and Pedersen (2017) demonstrated that the risk of a schizophrenia spectrum disorder diagnosis increases 15-fold in the year following a PTSD diagnosis and remains elevated for more than five years. This would suggest that PTSD symptoms themselves play a role in schizophrenia spectrum disorders, or that similar processes are involved in the genesis of these two disorders.

In addition to diagnostic and symptom overlap between PTSD and psychotic disorders/ auditory hallucinations, it has also been noted that there is significant similarity between the phenomenology of auditory hallucinations and trauma memory intrusions (a core feature of PTSD). Trauma memory intrusions and auditory hallucinations are both sensory-perceptual experiences with no objective, external stimulus and are experienced as involuntary and (often) to represent a current threat (Morrison et al., 2003). It is worth noting that trauma memory intrusions typically

take the form of visual images, whereas hallucinatory experiences are typically auditory experiences. However, trauma memory intrusions can also encompass other sensory modalities. A study of the phenomenology of trauma memory intrusions found that over half of people reported intrusions of auditory aspects of memories (Hackmann, Ehlers, Speckens, & Clark, 2004). Similar to trauma memory intrusions (that involve a direct reliving of aspects of the trauma memory) auditory hallucinations frequently have content that is identified as reflecting aspects of past adverse or traumatic events. An early study in this area examined case notes of 100 consecutive admissions to an acute psychiatric inpatient unit. Twenty-two of these patients had histories of physical or sexual abuse recorded in their notes and in this group half of the symptoms for which content was recorded in the notes appeared to be related to the abuse. However, with regard to auditory hallucinations, this was only based on seven patients who had sufficient information recorded (Read & Argyle, 1999). A more recent study synthesised data from 100 clinical cases in which the authors had used Romme and Escher's 'construct' method to formulate auditory hallucination content and characteristics in relation to life events (Corstens & Longden, 2013). This study found that 94% of participants' auditory hallucinations could be formulated as specific representations of social-emotional conflicts, most often resulting from interpersonal stress. However, it should be noted that the formulation of links between auditory hallucinations and traumatic events in this study was conducted as part of a therapeutic process, not under controlled research conditions. Additionally, the sample used were specifically people who had chosen to undertake this mode of therapy and were therefore likely to be self-selecting for those who had made links between their auditory hallucinations and past life events. The large phenomenological survey of auditory hallucinations conducted by McCarthy-

Jones et al. (2014) also found that 12% of people described their auditory hallucinations as identical replays of previous conversations they had heard, whilst 31% reported that the content was similar, but not identical. However, there was no assessment of whether these previous conversations were distressing or traumatic. An important and more methodologically robust study in this area examined descriptions of traumatic events and hallucinatory content from research interviews of 40 participants with current hallucinations and a history of traumatic events. Independent assessors rated the extracts to establish whether there were indirect (thematic) content links and direct (literal) content links. Direct content associations were found in 12.5% of participants and 57.5% had hallucinations with indirect (thematic) links with their trauma (Hardy et al., 2005). Despite some methodological issues with studies in this area, these findings do support the idea that (at least some) auditory hallucinations are similar to trauma memory intrusions in that they represent some kind of replay of trauma memory content.

The diagnostic, symptom, and phenomenological overlaps between PTSD and auditory hallucinations outlined in this section are suggestive of shared risk factors or psychological processes being involved in these experiences and this has increased interest in applying research and theory from the area of PTSD to understanding the causes of auditory hallucinations, particularly to understanding the mechanisms through which traumatic events may lead to auditory hallucinations.

4.2 Psychological theories of PTSD

Contemporary psychological theories of PTSD conceptualise the nature of information processing and memory encoding during traumatic events to be central to the development and maintenance of posttraumatic intrusions. Contextual binding has been implicated as a key aspect of adaptive information processing. Contextual

binding involves processing and encoding incoming information within a meaningful spatial and temporal context. Adaptive contextual binding during memory encoding leads to the ability to voluntarily recall a memory with intact associations to its temporal and autobiographical relevance. This binding of contextual information is considered to be central to the development of episodic memories (Tulving, 2002). Recent neurocognitive reviews have implicated contextual binding to be a central mechanism in the onset and maintenance of PTSD symptoms (Acheson, Gresack, & Risbrough, 2012; Liberzon & Sripada, 2007). Trait contextual memory deficits have been found to be common in people with PTSD and are also considered to be a risk factor for developing later PTSD (based on twin studies, prospective studies and studies of trauma exposed populations with PTSD and no PSTD). There is also robust evidence that hippocampal abnormalities are a risk factor for PTSD and underlie contextual binding deficits (Acheson et al., 2012).

Chris Brewin's influential 'dual representation' theory of PTSD (Brewin, 2001; Brewin, Gregory, Lipton, & Burgess, 2010), posits that normal, adaptive processing of an event involves the creation of two representations of a memory. Firstly, contextual representations (C-reps), which are representations of an event that include the spatial-temporal context associated with an episodic memory. These are available for voluntary retrieval and are integrated into personal semantic memory. C-reps are hypothesised to predominantly reflect hippocampal processing. Secondly, sensory representations (S-reps) represent a lower level of processing, dominated by perceptual information. S-reps are hypothesised to reflect predominantly amygdala-based processing of information. Brewin proposes that PTSD intrusions are caused as a result of S-reps of an extremely stressful event being created without association to corresponding C-reps, leading to memories that are difficult to recall voluntarily and

are vulnerable to being involuntarily triggered into consciousness. When these intrusions occur, they are experienced as a current perception rather than a retrieval of a memory. Dual representation theory has parallels with Ehlers and Clark's (2000) cognitive model of PTSD in which it is suggested that there is a shift in information processing style during traumatic events from 'conceptual processing' to 'data-driven-processing'. In conceptual processing, the meaning and context of a situation are encoded in an organised way, whereas data-driven processing predominantly encodes sensory impressions of an event. It is posited that data-driven processing during a traumatic event leads to memories that are poorly elaborated and inadequately bound with contextual information. These memories are sensitive to involuntary priming by matching triggers in the environment and are experienced in vivid sensory detail. In addition, they have no 'time tag' and are therefore experienced as a current threat.

Studies in both clinical and nonclinical populations have provided some evidence for the role of these information-processing styles the development of posttraumatic intrusions. Evidence for the role of data-driven processing in the development of PTSD was found in a prospective study of 176 survivors of a motor vehicle accident that showed data-driven processing to be a significant predictor of PTSD six months later (Murray, Ehlers, & Mayou, 2002). However, this study used a previously unvalidated measure of data-driven processing that only included two items. Similar results were found in a prospective study of 73 survivors of a physical assault, which demonstrated that cognitive processing during trauma (dissociation, data-driven processing, and lack of self-referent processing) predicted subsequent PTSD symptoms (Halligan, Michael, Clark, & Ehlers, 2003). Data-driven processing was also found to predict later PTSD in twenty survivors of the 2011 Christchurch earthquake (Hooper, Dorahy, Blampied, & Jordan, 2014). The role of data-driven

processing in trauma memory intrusions has also been explored in studies using analogue trauma paradigms in which people watch a film of a traumatic incident (usually the aftermath of a motor vehicle accident) and then are asked to measure the frequency of intrusions over the following week. Results from these studies have shown that people who report a data-driven processing style experience a higher number of intrusions of trauma film content (Halligan, Clark, & Ehlers, 2002; Laposa & Rector, 2012). Participant narratives of traumatic events have also been used to assess the nature of the encoded trauma memory as an indicator of the processing style engaged in during the event. A recent review noted some heterogeneity in results of research examining the nature of trauma narratives in relation to PTSD, but found robust evidence for trauma narratives in people with PTSD being dominated by sensory, perceptual and emotional details, which can be considered to be indicative of a 'data-driven' processing style (Crespo & Fernandez-Lansac, 2016).

There are some limitations in the body of research supporting information-processing models of PTSD. Studies have used heterogeneous methods to measure data-driven processing which raises issues for operationalising the construct itself and for comparing results between studies. Measures of data-driven processing also show significant correlations with other constructs such as peri-traumatic dissociation and self-referent processing, making it difficult to separate out the specific role of different aspects of information processing during traumatic events.

Information-processing models are not the only psychological theories of PTSD. Indeed, other models of PTSD do not place the nature of information processing during traumatic events as centrally, but instead focus on the role of associative learning and negative posttraumatic beliefs (Foa & Rothbaum, 1998). Despite there being a broad range of psychological theories of PTSD, psychological

theories of trauma-related auditory hallucinations that have drawn from the PTSD literature have tended to focus on information-processing theories. This has been because of the intersection of these ideas with information processing difficulties though to be inherent to psychotic disorders. These theories are described in the following section.

4.2 Psychological theories of auditory hallucinations that have been informed by theories of PTSD

Building on observations of significant comorbidity and phenomenological similarities between PSTD and psychotic disorders, Morrison et al. (2003) outlined a theory in which they conceptualised PTSD and psychosis not to be separate phenomena, but to be on a continuum of psychological outcomes following traumatic events. Morrison et al. hypothesised that the main difference between PTSD and psychotic disorders lay in the interpretation of intrusions. People would tend to be given a diagnosis of PTSD if they make a culturally acceptable appraisal of an intrusion (e.g. 'this is a trauma memory'), whereas a diagnosis of a psychotic disorder is more likely if someone makes a culturally unacceptable appraisal (e.g. 'this is the voice of the devil'). This theory was one of the first to identify that PTSD and psychotic experiences may have common causal pathways. The role of intrusions was also placed centrally in this model, however, there was no explicit exploration of mechanisms involved in the development of the intrusions themselves.

Recent theories have developed Morrison et al.'s conceptualisation, drawing further on theory and research from information processing models of PTSD to elucidate the precise mechanisms involved in trauma memory intrusions and psychotic symptoms. These theories have integrated cognitive psychology research

regarding the nature of episodic memory in people with psychotic disorders to explain why trauma memory intrusions may be experienced as auditory hallucinations.

It has long been proposed that disruptions to contextual integration in episodic memory are central to the experience of psychotic symptoms (Hemsley, 1994, 2005). Hemsley suggested that people with psychotic disorders have a weakened ability to integrate incoming information with both co-occurring information and stored information regarding past events. Thus, individuals with psychotic disorders are vulnerable to intrusions of decontextualised memories from long-term memory. Hemsley argues that these intrusions form the basis of positive symptoms of psychosis. Waters et al. (2006) also placed contextual binding disturbances centrally in their account of auditory hallucinations, theorising that deficits in contextual memory lead to memories being encoded without appropriate contextual cues signalling it to be a recollection of a past event. Additional difficulties in intentional inhibition mean that this decontextualised material intrudes into consciousness in an uncontrolled and unwanted fashion, thus forming the content of auditory hallucinations.

Fowler, Freeman, Steel, Hardy, and Smith's (2006) 'catastrophic interaction' hypothesis outlines how these trait weaknesses in contextual binding interact with the state shift to more data-driven processing during stressful or traumatic events, leading to intrusions of distressing, decontextualised material that then forms the basis of auditory hallucinations and other positive symptoms. Similarly, Steel, Fowler, and Holmes (2005) highlight that individuals who score high on measures of schizotypal personality exhibit trait weaknesses in contextual binding (Steel, Hemsley, & Pickering, 2002). This trait weakness in contextual binding is similar to the weakened contextual integration that occurs temporarily during traumatic events and that

contributes to posttraumatic trauma memory intrusions. It is suggested that these pre-existing difficulties in spatial and temporal integration therefore leave this group more vulnerable to frequent and distressing trauma memory intrusions following traumatic events (and perhaps even following more mundane daily stressors such as interpersonal conflict). Crucially, as a result of poor spatial and temporal integration, this group may also have more difficulties identifying intrusive material as a memory and are more likely to perceive it as external in origin, thus leading to auditory hallucinations.

Most recently, Amy Hardy (Hardy, 2017) has synthesised the latest research in the area to develop a multifactorial model of posttraumatic stress in psychosis. Hardy proposes two different pathways from trauma to psychotic experiences (including auditory hallucinations) with episodic memory, negative schematic beliefs, and emotion-regulation strategies differentially implicated in each pathway. The first pathway proposes that intrusions of trauma memory material form the basis of some psychotic experiences. These trauma memories occur on a contextualisation continuum, with the level of contextualisation depending on the nature of the memory encoding. Hardy conceptualises auditory hallucinations to be manifestations of particularly decontextualised trauma memories, thus they can be noted to have direct content links with traumatic events, but their lack of temporal-spatial contextualisation means that they are generally experienced without autonoetic awareness (remembering with a sense of self-recollection). The second pathway proposes that some auditory hallucinations are not directly linked to episodic memory, but instead represent auditory images (or anomalous experiences). These voices have indirect links to trauma as their content and appraisals are shaped by beliefs about the self and others abstracted from traumatic events and stored in autobiographical

memory. They are also influenced by regulation strategies developed as survival mechanisms during trauma, such as dissociation, avoidance, and hypervigilance, given the impact of these processes on sensory-perceptual processes. A strength of this theory is its ability to integrate a number of posttraumatic processes that have been implicated in the development of psychotic symptoms following traumatic events. It is also able to explain the fact that auditory hallucinations differ in how directly their content reflects things that were experienced at the time of the traumatic event. As outlined previously, a small number of people experience auditory hallucinations that are a direct replay of things heard at the time of their trauma (12.5%; Hardy et al., 2005). Hardy proposes that this type of auditory hallucination is caused by the episodic memory pathway. In contrast, many people (57.5%) experience auditory hallucinations with indirect, or thematic content links to past traumatic events (Hardy et al., 2005), likely manifestations of the anomalous experience pathway (and shaped predominantly by negative schematic beliefs rather than episodic memory).

4.3 Research relating to PTSD symptoms, trauma memory processing, and auditory hallucinations

There is a growing body of evidence to support the theories outlined in Section 4.2. Firstly, there is preliminary evidence that weakened trait contextual binding in people scoring high on schizotypal traits contributes to a data-driven peritraumatic processing style and that this leads to increased posttraumatic intrusions. Individuals scoring high on schizotypal traits have been found to report more intrusions in the week following watching a distressing film (Holmes & Steel, 2004) and in a group awaiting treatment in a traumatic stress clinic (Marzillier & Steel, 2007). In addition, an association between high schizotypy, data-driven

processing and increased posttraumatic intrusions was found in motor vehicle accident survivors (Steel, Mahmood, & Holmes, 2008). People with anomalous experiences (such as auditory hallucinations), without a need for care, have also been found to have higher levels of data driven processing and intrusions following exposure to a trauma film (Marks, Steel, & Peters, 2012). In a prospective study of people who had experienced a physical assault, Geddes, Ehlers, and Freeman (2016) found that cognitive processing styles implicated in PTSD (self-referential processing in particular) were significant predictors of later hallucinatory experiences. There is therefore evidence to support the predicted relationship between weakened trait contextual binding, data-driven processing, and trauma memory intrusions in nonclinical populations, however this has not yet been tested in populations with clinical psychotic experiences.

A number of studies have found a relationship between posttraumatic stress symptoms implicated in Hardy's (2017) model (trauma memory intrusions, negative posttraumatic beliefs, and emotion regulation strategies) and hallucinations. Gracie et al. (2007) found a significant association between trauma memory intrusions and hallucinatory experiences in a general population sample. A large population survey (n=7,403) also found that trauma memory intrusions were a significant predictor of auditory hallucinations (Alsawy, Wood, Taylor, & Morrison, 2015). Bendall et al. (2013) found a positive relationship between trauma memory intrusions and hallucinations, however this did not reach significance (likely due to lower power to detect an effect, n=13). In an early psychosis sample (n= 66), Peach et al. (2018) reported that posttraumatic intrusions and negative posttraumatic beliefs mediated the relationship between childhood trauma and hallucinations. In addition, post-traumatic intrusions were independently associated with hallucination severity.

In contrast, a cross-sectional study conducted with a sample of people with a psychotic disorder (*n*= 228) and found that the relationship between childhood sexual abuse and hallucinations was mediated by numbing and hyperarousal, but not intrusive trauma memory, or negative posttraumatic beliefs (Hardy et al., 2016). Similarly, in a cross-sectional study with a group of 328 predominantly African American people, Powers et al. (2016) found that current PTSD was a predictor of psychotic disorder. When PTSD symptom clusters were analysed separately, avoidance and numbing were found to have a unique association with psychotic disorders. Negative posttraumatic beliefs have been found to mediate the relationship between trauma and hallucination proneness in a nonclinical sample (Gracie et al., 2007) and to predict hallucinatory experiences following a physical assault (Geddes, Ehlers, & Freeman, 2016). A recent systematic summarised evidence for different posttraumatic psychological processes as mediators in the trauma-psychosis relationship and confirmed that the strongest evidence to date is for three main processes: posttraumatic sequelae, affective dysfunction and dysregulation, and maladaptive cognitive factors (i.e. those outlined in Hardy's model).

A significant limitation of evidence in this area is that studies to date have predominantly been cross-sectional. Cross-sectional data are limited in exploring the theorised relationships between trauma memory processing, PTSD symptoms, and hallucinations in two main ways. Firstly, cross-sectional studies can only infer association between variables, limiting causal inferences. Secondly, cross-sectional studies take a snapshot of aggregated measures of variables at a single time point and therefore do not capture dynamic moment-to-moment relationships between these experiences that are implied by psychological theories. The methodological

limitations with current evidence in this area is explored in more detail in Chapter

Five in an opinion paper (the first peer reviewed publication).

Despite these limitations, as suggested by a number of theories (Fowler et al.,

2006; Hardy, 2017; Morrison et al., 2003; Steel et al., 2005), evidence does point

towards a role for PTSD symptoms and trauma memory processing in the genesis of

some auditory hallucinations. In line with a 'process-based' approach to treating

auditory hallucinations in which psychological therapies are developed to target

specific putative psychological mechanisms, this raises an important opportunity for

the development of new psychological intervention strategies for auditory

hallucinations. Specifically, there are a number of well-evidenced psychological

therapies for PTSD that have a focus on trauma memory processing. It is possible that

these therapies may also have a therapeutic impact on some auditory hallucinations.

This would also be in line with calls from people with lived experience of auditory

hallucinations for the development of psychological therapies that are able to address

the role of past traumatic events (Corstens et al., 2014).

4.6 Trauma-focused treatments for PTSD

Psychological treatments for PTSD are well established. Specifically, trauma-

focused interventions, including prolonged exposure (PE), trauma-focused CBT and

eye movement desensitisation and reprocessing therapy (EMDR) have strong

evidence for their effectiveness in treating PTSD (Bisson et al., 2007) and are

recommended as first line treatments for PTSD in adults (National Institute of Clinical

Excellence, 2018; Phoenix Australia, 2013). All evidence-based therapies for PTSD

have been identified to share common components and aims, but these are

emphasised to varying degrees in each specific protocol (Schnyder et al., 2015).

Firstly, all protocols involve some element of *psychoeducation* about the nature and

course of PTSD. *Coping skills and emotion regulation strategies* are usually taught (sometimes explicitly within the protocol, sometimes more implicitly). A key component of all evidence-based therapies for PTSD is *imaginal exposure*, in which people are exposed to the memory of the traumatic event, often (but not always) in the form of picturing the event in imagination and verbalising a present tense, first person narrative of the event. *Cognitive processing, restructuring or meaning making* (in which people are encouraged to reappraise unhelpful beliefs about the traumatic event or its aftermath in light of new evidence) can also be found in the majority of evidence-based interventions. All therapies target *emotions* to some extent – with differing focuses on fear, guilt, shame, anger, grief or sadness. *Memory processes* are considered to play a role in all evidence- based PTSD treatments, with the reorganisation of memory functions and the creation of a coherent trauma narrative forming central goals of all trauma-focused therapies.

Despite the efficacy of trauma-focused therapies for PTSD, it is worth noting that there are some concerns in the literature regarding implementation and therapy dropout. It is well documented that real life delivery of evidence-based trauma-focused therapies for PTSD is low. Becker, Zayfert, and Anderson (2004) surveyed psychologists and found that less than 20% were using evidence-based trauma-focused therapies when treating PTSD. Respondents reported that fears about symptoms exacerbation and client dropout impacted on their decision to use trauma-focused therapies. Randomised controlled trials of evidence-based trauma-focused therapies have found dropout rates to be between 20 to 27% (Hembree et al., 2003). However, randomised trials are often selective in their inclusion and exclusion criteria (often excluding more complex cases) and use well supervised, expert clinicians. Dropout rates seen under these conditions are likely to be at the lower end of that seen

when therapies are implemented in real world practice. Indeed, there have been reports of much higher dropout rates in routine practice, for example Mott et al. (2014) examined treatment completion of PE or cognitive processing therapy for PTSD in a U.S. veterans' affairs clinic and found that only 8% of participants completed a recommended course of treatment. These implementation and dropout issues suggest that feasibility and acceptability are important factors to consider in developing and trialling trauma-focused therapies.

There are different (though overlapping) schools of thought regarding the mechanisms through which trauma-focused therapies improve PTSD symptoms. Proponents of PE (one of the best evidence therapies for PTSD that involves exposure to trauma memories and reminders for a prolonged period of time) hypothesise that fear habituation and the reduction of negative posttraumatic beliefs are key mechanisms of change (Foa & Rothbaum, 1998). An empirical review of mediators of change in PE therapy trials did indeed find that the strongest evidence was for belief change and between-session habituation (Cooper, Clifton, & Feeny, 2017). Information processing accounts of PTSD propose that trauma-focused therapies operate through the elaboration and contextualisation of the memory and the updating of unhelpful peri and posttraumatic cognitions that are maintaining a current sense of threat (Brewin, Gregory, Lipton, & Burgess, 2010). There is good evidence for changes in PTSD related cognitions being a key mechanism of change across different trauma-focused therapies (Zalta, 2015). There is currently limited evidence regarding how the nature of trauma memories change during trauma-focused therapies and whether this is a mediator of treatment outcome. Measuring aspects of memory processing is challenging, but existing studies have attempted to do this using either self-report measures or objective coding of trauma narratives. In a small study (n=22),

intrusive memories of traumatic events were found to decrease in self-reported

frequency, vividness, and 'nowness' (all considered to be markers of predominantly

perceptual, decontextualised memories) over a course of cognitive therapy for PTSD

(Hackmann et al., 2004). One small study that rated aspects of trauma narratives at

the beginning and the end of trauma-focused therapies found evidence that thoughts

that reflected attempts to organise the trauma memory increased over therapy and that

decreases in the fragmentation of trauma narratives correlated with reductions in

trauma-related symptoms (Foa, Molnar, & Cashman, 1995). However, an attempted

replication of these findings found that participants who had responded well to PE

therapy did not differ from those who had not responded well in terms of memory

fragmentation or organised thoughts (Minnen, Wessel, Dijkstra, & Roelofs, 2002).

Studies examining changes in trauma memories as a result of trauma-focused

therapies and whether these changes mediate outcome have been limited by small

samples and have used varying methods of measuring this construct. It is clear that

further research is needed in this area to clarify whether predictions made by

information processing theories of PTSD regarding the mechanisms of change in

trauma-focused therapy are supported.

4.7 The use of trauma-focused therapies in psychosis populations

The majority of treatment trials of trauma-focused therapies for treating PTSD

have used the presence of psychotic disorders as an exclusion criterion. This

exclusion was due to concerns that people with psychosis would not be able to

tolerate these intensive treatments because of their increased sensitivity to stress and

may therefore experience symptom exacerbation and/or increased risk if given these

therapies. This meant that for many years there was a paucity of data regarding the

effectiveness of these treatments for people experiencing psychosis. More recently,

however, following increased recognition of the prevalence of PTSD in this population (de Bont et al., 2015) there have been several randomised controlled trials assessing the efficacy of different trauma-focused therapies in populations with psychotic disorders. The third peer reviewed publication from this thesis (Chapter 9) presents a systematic review and meta-analysis of all of the studies to date that have used trauma-focused therapies to treat comorbid PTSD in people with psychotic disorders and this literature will therefore be described in detail then. For the purpose of this chapter, it is worth noting that studies have found that exposure-based trauma-focused therapies (PE and EMDR) are effective at treating PTSD symptoms and do not lead to psychotic symptom exacerbation or adverse events (van den Berg et al., 2015a, 2015b). However, trials that have used adapted protocols (not including direct exposure to the trauma memory, but focusing on cognitive restructuring) have had less positive findings (Mueser et al., 2015; Mueser et al., 2008; Steel et al., 2017).

Despite the positive findings under randomised controlled trial conditions, potential issues with the use of trauma-focused approaches in psychosis populations have also been highlighted. Firstly, there may be issues with the implementation of these approaches, with clinicians reporting reluctance in the assessment and treatment of trauma related difficulties in an early psychosis population due to concerns about symptom exacerbation and safety (Gairns, Alvarez-Jimenez, Hulbert, McGorry, & Bendall, 2015). Secondly, there are some reports of symptom exacerbation and significant distress within young people with a first episode of psychosis receiving a trauma therapy (though this was not related to poor outcomes at the end of therapy (Tong, Simpson, Alvarez-Jimenez, & Bendall, 2017)). These potential feasibility and acceptability issues will need further investigation when exploring the use of these therapies within psychosis populations.

4.8 The use of trauma-focused therapies to treat psychotic symptoms

To date, there is a small body of published literature that has explored the use of trauma-focused therapies to specifically target auditory hallucinations. Keen, Hunter and Peters (2017) used an integrated trauma-focused therapy to treat both PTSD and psychotic symptoms in a case series (*n*=9). The therapy was a 'phase based' approach, which included 1) assessment, engagement and goal setting, 2) stabilisation and coping strategy enhancement, 3) formulation, 4) integrated psychosis and trauma-focused interventions (including cognitive restructuring, imagery rescripting, reliving with cognitive restructuring and schema work). Participants received a median of 41 sessions (range 25 to 66). Notably, this study focused exposure-based memory work for memories that were related to PTSD intrusions, but generally used cognitive restructuring to address auditory hallucinations. The study had no dropouts from therapy and no participants had a reliable worsening of symptoms. Findings were generally positive, with 63% of participants achieving reliable improvement for PTSD symptoms, 25% for auditory hallucinations, and 50% for delusions. This study provides some indication of the impact of trauma-focused therapies for auditory hallucinations, suggesting that a small group of people benefit, it is not clear which aspects of the therapy had a positive impact, and the memory processing part of the therapy did not focus on memories related to auditory hallucinations per se.

Paulik, Steel, and Arntz (2019) report results from an imagery rescripting intervention specifically targeting trauma memories that are related to auditory hallucination content. In a single arm open trial case series design, 12 participants with auditory hallucinations that were thematically related to past trauma undertook an eight-session imagery rescripting intervention. Imagery rescripting is a trauma-

focused therapy in which the client is guided to imagine alternative, endings to their trauma memories in which their needs are met. Imagery rescripting involves a degree of exposure to the trauma memory but does not involve direct exposure to the most distressing aspects of the memory (the rescript begins before this point in the memory is reached). Results showed significant reductions in trauma memory intrusions and auditory hallucination distress and frequency. The therapy was also well tolerated, with only one person dropping out of therapy. As the first published study to explore the effects of a trauma-focused therapy for auditory hallucinations that specifically targets traumatic events related to auditory hallucination content, this trial suggests that there is promise in this approach. The authors justify the use of imagery rescripting because it can lead to change in beliefs that can generalise over a number of trauma memories (potentially useful in this context because auditory hallucinations are typically thematically related to repeated traumatic events). However, imagery rescripting does not yet have a robust evidence base for the treatment of PTSD as a standalone treatment. Imagery rescripting is thought to act at a level of belief change and does not have the elaboration and contextualisation of trauma memories as a primary aim (though this may happen as a result of accessing the memories). Given the potential role of PTSD symptoms and trauma memory processing in auditory hallucinations outlined so far in this thesis, it may be that therapies that specifically target these processes (i.e. those that explicitly focus on exposure to the trauma memory) have more potent effects on auditory hallucinations.

4.9 Chapter Summary

There is significant diagnostic, symptom, and phenomenological overlap between PTSD and psychosis (including auditory hallucinations). This has led to the development of number of psychological theories of auditory hallucinations that have

drawn upon literature regarding psychological mechanisms involved in PTSD. Particularly, theories have suggested that auditory hallucinations are a type of trauma memory intrusion that is particularly decontextualised. Posttraumatic avoidance and hyperarousal and negative posttraumatic beliefs have also been implicated. The majority of evidence in support of these theories is derived from cross-sectional data and there is a need to extend on these methods in order to understand the moment-to-moment relevance of PTSD symptoms and trauma memory processing and to test their causal role. The potential role of PTSD symptoms and trauma memory processing in auditory hallucinations also offers an important opportunity for intervention development, since there are well-evidenced psychological therapies for PTSD that are posited to act on these mechanisms. There is some evidence that trauma-focused therapies are safe and effective in treating comorbid PTSD in people with psychosis. There are two small studies testing trauma-focused therapies to specifically treat trauma-related auditory hallucinations, however these studies have not had a central focus on exposure to the trauma memory, an intervention component posited to be most potent in addressing trauma memory intrusions and contextualising the trauma memory.

Chapter Five: Can We Use an Interventionist–causal Paradigm to Untangle the

Relationship between Trauma, PTSD and Psychosis? (Publication One)

5.1 Preamble to Publication One

Publication One was the culmination of a period of time spent reviewing the literature and considering methodological approaches that might advance research in understanding the role of PTSD symptoms and trauma memory processing in trauma-related auditory hallucinations. In this opinion piece it was argued that the field needed to progress beyond studies of association to using experimental designs. Specifically, this publication outlined the interventionist–causal paradigm, as a model that would help to further knowledge relating to the causal role that PTSD symptoms and trauma memory processing play in trauma-related auditory hallucinations, and also in evaluating the potential for trauma-focused psychological therapies as a treatment for trauma-related auditory hallucinations (the overarching aim of this thesis).

Publication One has been published in the journal *Frontiers in Psychology*, which is a highly ranked, open access, international journal. The 2018 impact factor of *Frontiers in Psychology* was 2.129. A copy of the article in its published form is provided in Appendix II. The 'Author Indication Form', which details the nature and extent of the candidate and co-authors' contributions to this manuscript is included in Appendix III. The complete citation is as follows:

Brand, R.M., Rossell, S.L., Bendall, S., and Thomas, N. (2017). Can we use an interventionist–causal paradigm to untangle the relationship between trauma, PTSD and psychosis? *Frontiers in Psychology*, 8: 306. doi:10.3389/fpsyg.2017.00306.

5.2 Introduction

There is mounting evidence that exposure to traumatic or adverse life-events is associated with increased risk of psychosis (Bendall et al., 2010; Bendall et al., 2008; Read & Bentall, 2012; Read et al., 2001). However, to inform treatment and prevention, it is necessary to go beyond association to understand *how* traumatic experiences may lead to the development of psychotic symptoms. In this paper, we argue that doing so requires the identification of biological, psychological and social processes that may be involved in the observed trauma–psychosis relationship, and determining which are causally related. We propose that this can be done in conjunction with focused intervention procedures that may test theoretical mechanisms, in parallel with piloting potential components of therapeutic interventions.

A recent proliferation of research has examined a broad range of factors as putative causal mechanisms. One important strand of this research has drawn on the particular relationship between trauma, posttraumatic stress disorder (PTSD) and psychosis. PTSD is one of the most rigorously researched sequelae of trauma exposure and is, by definition, caused by traumatic events. There are high rates of comorbidity between PTSD and psychosis (Anketell et al., 2010; Kilcommons & Morrison, 2005; Sareen et al., 2005), and PTSD is a risk factor in the subsequent development of psychosis (Okkels et al., 2017). This relationship may provide an insight into the mechanisms through which trauma exposure can lead to the emergence and maintenance of psychosis.

To make causal inferences regarding these putative mechanisms, the literature needs to move beyond establishing association to experimental studies in which trauma exposure, PTSD symptoms or causal mechanisms involved in PTSD, are

subject to controlled manipulations. However, there are feasibility and ethical issues in this undertaking and we therefore propose that a research paradigm referred to as the interventionist–causal approach offers a critical way forward. We pay particular attention to trauma-related psychological mechanisms, with a view that a more sophisticated understanding of the causal role of these mechanisms will lead to much needed improvements in psychological interventions for psychosis (Freeman, 2011; Thomas et al., 2014). While identifying causal mechanisms is not the only way of addressing recovery, this process of intervention development can add value to broader intervention approaches. Indeed, this process has been helpful in refining and improving the efficacy of psychological interventions for anxiety (Clark, 2004).

5.3 Mechanisms linking PTSD and psychosis

Mueser and colleagues (Mueser, Rosenberg, Goodman, & Trumbetta, 2002) proposed that PTSD symptomatology itself mediates the relationship between trauma exposure and the course of serious mental illness, particularly schizophrenia. Whilst not commenting on whether PTSD plays a causal role in the development of psychosis, this theory places PTSD symptomatology centrally in understanding the exacerbation of psychotic symptoms.

Morrison et al. (2003) went further, proposing that rather than being separate, psychotic symptoms and PTSD fall on a continuum of trauma-related reactions and are caused and maintained by similar psychological mechanisms. Researchers have since further elucidated psychological mechanisms involved in specific symptoms of psychosis that may be shared with those involved in PTSD. The correlation between posttraumatic intrusions and hallucinations in trauma-affected populations (Alsawy et al., 2015; Ayub, Saeed, Kingdon, & Naeem, 2015; Gracie et al., 2007) and the fact that the content of hallucinations often have thematic or direct links with trauma

content (Corstens & Longden, 2013; Hardy et al., 2005; McCarthy-Jones et al., 2014; Read, Agar, Argyle, & Aderhold, 2003) has led to the proposal that some hallucinations may in fact be a form of posttraumatic intrusion. Contemporary psychological theories of PTSD conceptualise the nature of cognitive processing during traumatic events to be central to the development of posttraumatic intrusions (Brewin, 2001; Brewin et al., 2010; Ehlers & Clark, 2000). Shifts in information-processing style during traumatic events are posited to lead to trauma memories that are decontextualised, fragmented, dominated by sensory information, and sensitive to involuntary priming. The nature of cognitive processing during traumatic events has also been implicated in the development of hallucinations in the general population (Geddes et al., 2016) and in people high in schizotypy (Steel et al., 2005).

Dissociation, another psychological process implicated in PTSD, has also been linked to hallucinations following trauma. Indeed, many researchers propose that hallucinations are dissociative phenomena (Longden et al., 2012; Moskowitz & Corstens, 2007). Dissociation is correlated with hallucinatory experiences (Pilton et al., 2015), mediates the relationship between childhood trauma and hallucinations (Perona-Garcelán et al., 2012; Varese, Barkus, et al., 2012) and predicts hallucinations in the flow of daily life (Varese et al., 2011).

Hallucinations are not the only psychotic symptom that has been linked to PTSD symptoms and related mechanisms. Associations between delusional beliefs and PTSD symptoms have been observed following traumatic events (Ayub et al., 2015; Freeman et al., 2011) and the same cognitive factors have been found to predict both paranoia and PTSD following a physical assault (Freeman et al., 2013). Research has been more equivocal with regards to negative symptoms (Lysaker & LaRocco, 2008; Resnick, Bond, & Mueser, 2003; Strauss, Duke, Ross, & Allen, 2011; Vogel et

al., 2011) but it has been suggested that these can be manifestations of the avoidance of traumatic memories (McGorry, 1991; Morrison et al., 2003; Stampfer, 1990).

In summary, there is evidence of a close relationship between PTSD and psychotic experiences, but questions remain regarding whether PTSD symptomatology itself represents a causal mechanism in the development or maintenance of psychosis, or whether shared mechanisms underpin the causal relationships between trauma and both PTSD and psychosis outcomes. Establishing causal inferences regarding psychological mechanisms involved in psychosis is, of course, complex. Symptoms are likely to be caused by multiple mechanisms and each mechanism is likely only to contribute to the probability of a symptom occurring. Nonetheless, identifying the potential role of each PTSD-related psychological mechanism in the development and maintenance of psychosis will inform more evidence-driven and targeted psychological interventions for trauma-related psychoses. A particularly tantalising aspect of the relationship between PTSD and psychosis is that there are already well-established, effective treatments for PTSD. If psychological mechanisms involved in PTSD do play a causal role in psychotic experiences, this would open up promising new treatments for psychotic symptoms.

5.4 Beyond association to identifying causal mechanisms

In order to establish the causal role of candidate mechanisms, certain criteria must be met. Despite a lack of consensus on the precise definition of causality, epidemiologists have outlined the essential properties of causal relationships; namely, that there is an association between the variables, that the cause temporally precedes the effect, that change in the putative causal variable leads to change in the outcome, and that spurious, confounding variables in this relationship are controlled for (also referred to as sole plausibility; Reininghaus, Depp, & Myin-Germeys, 2016).

Thus far, research in the field has predominantly involved cross-sectional studies that examine associations between trauma, PTSD, psychosis, and putative shared mechanisms. Cross-sectional studies are, however, limited in drawing causal inferences, since it is not possible to robustly establish temporal relationships and sole plausibility. There are also examples of prospective studies in the area, which have built on these cross-sectional associations by establishing temporal ordering (Okkels et al., 2017). However, prospective studies can be time intensive and still do not offer control over extraneous variables to establish sole plausibility. Observational studies that observe natural fluctuations in putative mechanisms and how these interact with symptoms have also made recent valuable additions to the literature, particularly with the use of mobile technology in ecological momentary assessment studies (e.g. Varese et al., 2011). Yet, without controlled manipulation of variables it is again difficult to establish sole plausibility (Reininghaus et al., 2016).

We argue that what is now needed are experimental approaches using controlled manipulations of trauma exposure, PTSD symptoms, or putative shared causal mechanisms and an assessment of the impact of these manipulations on psychotic symptoms. There have been initial examples of this in the use of the analogue trauma paradigm, in which trauma exposure is experimentally manipulated (with the presentation of a distressing film) and outcomes examined (e.g. Marks et al., 2012). There are, however, challenges in the design and execution of these studies in trauma-affected and psychosis populations, possibly explaining why the majority of these studies have thus far been conducted with nonclinical samples. In clinical groups, there are ethical and clinical issues with introducing trauma exposure as an independent variable, or with inducing controlled increases in PTSD symptoms.

5.5 An interventionist–causal paradigm for the investigation of the relationship between trauma, PTSD and psychosis

We propose that an alternative experimental model that holds promise in moving past this methodological impasse is the interventionist–causal paradigm. In this approach, causation is substantiated by controlled manipulation of the hypothesised causal mechanism and examination of the subsequent effect on the symptom of interest (Kendler & Campbell, 2009). In psychiatry research this can be accomplished using interventions proposed to act on causal mechanisms, establishing their effect on these mechanisms when compared with a control intervention to minimise other confounding variables, and observing the impact on the symptoms of interest. If this chain of causality can be established, then causal inferences regarding the mechanisms in question may be confirmed. In practice, this looks like a randomised controlled trial of an intervention, but as well as establishing treatment efficacy, we use this paradigm to further our understanding of causal mechanisms. An interventionist–causal paradigm has been previously noted for its use in understanding causal mechanisms in psychosis (Freeman, 2011; Garety & Freeman, 2013; Reininghaus et al., 2016). An attractive aspect of this model is that the experimental intervention is one that is designed to reduce problematic causal processes and thus (hypothetically) improve symptom outcomes of interest. This is well aligned with the ethos of the fields of clinical psychology and psychiatry.

The well-developed PTSD treatment literature gives us a head start in terms of assessing the causal role of PTSD symptomatology itself in psychotic experiences using the interventionist–causal model. Treatments that are already known to be effective in reducing PTSD symptoms, such as PE, trauma focused CBT and EMDR (Bisson et al., 2007), can be delivered to people with psychosis in controlled studies

and the effects on both PTSD symptoms and psychotic symptoms established. Approaches to date using these treatments for people experiencing psychosis have focused on treating comorbid PTSD symptoms, demonstrating the safety of using such interventions and some positive effects on PTSD symptoms, particularly for EMDR and PE (van den Berg et al., 2015a), but less so for cognitive restructuring (Steel et al., 2017). There is, however, limited data on the impact of these interventions on psychotic symptoms.

Additionally, the putative shared mechanisms involved in both PTSD and psychosis can be subject to interventionist–causal enquiry using specific components of psychological interventions, ascertaining that they act on a mechanism of interest, and observing the effect on psychotic symptoms. This is somewhat more complex, since literature regarding the mechanisms of action of psychological treatments remains in its infancy, however the interventionist–causal model is well placed to deal with this complexity in separating specific mechanisms of action and their relationship to treatment outcomes. A promising example of this, a pilot trial of a brief CBT intervention for depersonalisation in psychosis, is currently underway (Farrelly, Peters, Azis, David, & Hunter, 2016). We propose that this paradigm now needs to be extended to the multitude of other potential causal mechanisms implicated in PTSD and psychosis. Table 1 outlines interventions or intervention components that may be explored in an interventionist–causal model to explicate the causal role of these mechanisms.

Table 1. Putative causal mechanisms involved in both PTSD and psychosis and interventions with which the interventionist–causal paradigm can be used to examine causality

Putative mechanism	Intervention
Trauma memory processing	Imaginal exposure, EMDR
Negative posttraumatic beliefs	Trauma-focused cognitive therapy, cognitive processing therapy
Dissociation	Cognitive behavioural interventions for dissociation
Posttraumatic avoidance	In vivo and imaginal exposure

In summary, we believe that interventionist–causal models offer a crucial next step in untangling the relationship between trauma, PTSD and psychosis. Importantly, the paradigm offers a way of extending our understanding beyond that of association, into establishing causal inferences. In addition, research of this nature can establish individual treatment components, acting on specific causal mechanisms, which can effectively be used to treat psychotic experiences in those who have experienced trauma.

5.6 Reflection on Publication One

The methodological issues explored in Publication One crystallised the methodology that was used in the empirical studies making up this thesis. Specifically, based on the argument made in Publication One, Study Two and Study Three aimed to provide initial data in line with the interventionist–causal approach and to pave the way for a larger, well powered interventionist–causal study using a randomised controlled trial. The literature reviewed in this opinion piece also highlighted EMA as a promising methodology that would move beyond cross-sectional studies of association between PTSD symptoms and auditory hallucinations, thus shaping the design of Study One.

Chapter Six: Where Do We Go from Here? A Road Map for the Programme of Research in This PhD

Part one of this thesis has provided a review of relevant literature in the area of auditory hallucinations, trauma, and PTSD to provide background context and introduce the rationale for the current thesis. The present chapter aims to summarise key points from this literature review and highlight gaps and priorities. The overarching aim of this thesis will then be introduced as an important step towards addressing the gaps and priorities identified.

6.1 Summary of the literature review

Auditory hallucinations occur transdiagnostically and are a common and often distressing experience. Despite clinical need, our best-evidenced psychological therapies for auditory hallucinations currently only have small to moderate effects. *There is a need to improve the efficacy of psychological therapies for distressing auditory hallucinations.*

A symptom-focused approach that focuses on empirically derived mechanisms underpinning auditory hallucinations may improve the efficacy of therapies. To date psychological therapies for auditory hallucinations have focused primarily on one mechanism of interest (beliefs about power and omnipotence), despite a growing understanding of other putative psychological mechanisms involved in auditory hallucinations.

Current state of the art empirical evidence regarding psychological mechanisms underpinning auditory hallucinations needs to be translated into new psychological therapies for auditory hallucinations.

There is growing evidence that traumatic life events play a role in psychotic symptoms, including auditory hallucinations. Diagnostic, symptom, and

phenomenological overlaps between PTSD and auditory hallucinations have led researchers to examine the role of PTSD symptoms and trauma memory processing as key psychological mechanisms in the link between traumatic events and auditory hallucinations. There is increasing evidence to support the theory that some auditory hallucinations are a form of trauma memory intrusion that is particularly decontextualised. Evidence also suggests that posttraumatic beliefs and emotion regulation strategies (hyperarousal, avoidance, and numbing) play a role. However, this evidence is predominantly cross-sectional and therefore is limited in drawing causal inferences and in explaining the moment-to-moment dynamic relationship between these experiences and auditory hallucinations that is implied by psychological theory.

Research examining PTSD symptoms and trauma memory processing as putative mechanisms needs to move beyond association to explicate dynamic moment-to-moment relationships and strengthen causal inferences.

Given the potential role of trauma memory processing and PTSD symptoms in some auditory hallucinations, there is a possibility that trauma-focused therapies for PTSD that are known to ameliorate these factors may be a helpful treatment for auditory hallucinations. There is limited evidence of the effects of these therapies on psychotic symptoms and on auditory hallucinations specifically. Two small studies that have examined the effects of trauma-focused therapies for trauma-related auditory hallucinations have not had a central focus on exposure to the trauma memory, an intervention component posited to be most potent in addressing trauma memory intrusions and contextualising the trauma memory.

There is a need to explore the potential of exposure-based trauma-focused therapies in treating auditory hallucinations that may be related to traumatic events.

6.2 Overarching aim of this thesis

This thesis builds upon the research literature reviewed in Part One, focusing on the gaps and priorities identified and addressing one overarching aim: to explore the role of PTSD symptoms and trauma memory processing as potential psychological mechanisms involved in auditory hallucinations, and as a potential target for treatment using trauma-focused psychological therapies.

6.3 Empirical studies addressing this aim

Three novel empirical studies were designed to address this aim:

6.3.1 Study One: An EMA study to examine the moment-to-moment relationship between PTSD symptoms and auditory hallucinations in daily life.

Study One used an EMA methodology in order to extend upon previous (primarily cross-sectional) research that has indicated that PTSD symptoms and trauma memory processing play a role in trauma-related auditory hallucinations. Multilevel modelling of EMA data in this study was able provide novel insights into the dynamic, moment-to-moment associations between PTSD symptoms and auditory hallucinations in daily life. The study also aimed to identify between-person factors (moderators) that influence the relationship between posttraumatic stress symptoms and auditory hallucinations. Based on trauma-informed theories of auditory hallucinations (Fowler et al., 2006; Hardy, 2017; Steel et al., 2005) hypothesised moderators were: content links between auditory hallucinations and traumatic events, the nature of the trauma memory, and PTSD diagnostic status.

6.3.2 Study Two: A meta-analysis examining whether trauma-focused therapies delivered to treat comorbid PTSD in psychosis populations have a secondary effect on psychotic symptoms.

There are a number of treatment trials that have examined the effects of trauma-focused therapies in treating comorbid PTSD in populations with psychotic disorders. Prior to this study there had been no systematic synthesis of the secondary effects of these treatments on psychotic symptoms (including auditory hallucinations). The meta-analysis conducted for Study Two therefore provided novel data on the potential effects of using trauma-focused therapies in treating psychotic symptoms. Additionally, in the spirit of the interventionist–causal model, the results of this meta-analysis provided indications regarding the causal role of PTSD symptoms and trauma memory processing in psychotic symptoms (since applying an intervention that reduces PTSD symptoms and processes the trauma memory would be expected to reduce psychotic symptoms if there is a causal relationship).

6.3.3 Study Three: A pilot trial assessing the feasibility, acceptability and potential effects of an exposure-based trauma-focused therapy for trauma-related auditory hallucinations.

Study Three was a pilot trial of an exposure-based trauma-focused therapy component, imaginal exposure, that targeted PTSD symptoms and trauma memory processes as putative psychological mechanisms involved in trauma-related auditory hallucinations. Given some prior evidence of implementation and safety issues in using trauma-focused therapies in a psychosis population (Gairns et al., 2015; Tong et al., 2017) and the fact that this was a novel application of these therapies (i.e. to specifically treat auditory hallucinations), pilot data regarding feasibility, acceptability and potential effects were needed. The pilot data from this study also provide a basis

for larger trials that can robustly assess the efficacy of these interventions and assess the causal role of PTSD symptoms and trauma memory processing in auditory hallucinations using an interventionist–causal model.

PART II: EMPIRICAL STUDIES

Chapter Seven: Methods

The three empirical studies that form this thesis are presented as four peer-reviewed publications within Chapters Eight, Nine, Ten, and Eleven. These manuscripts provide details regarding the hypotheses, design, and methods used in these empirical studies. However, due to the limited scope of peer-reviewed journal articles, these manuscripts do not provide detailed description of some of the more nuanced methodological decisions that were made. This chapter aims to provide an overview of the design of each study as well an exploration of key methodological and analytical decisions that were not explored in depth within the scope of the peer-reviewed articles. The studies have been ordered to provide a logical flow to the thesis, with Study One being an EMA study examining the moment-to-moment relationship between PTSD symptom and auditory hallucinations in daily life, Study Two being a meta-analysis examining whether trauma-focused therapies delivered to treat comorbid PTSD in psychosis populations have a secondary effect on psychotic symptoms, and Study Three being a pilot trial assessing the feasibility, acceptability and potential effects of an exposure-based trauma-focused therapy for trauma-related auditory hallucinations. Despite the separation of the studies into this linear order, it should be noted that in reality Study One and Study Three occurred concurrently, with Study One being partially nested within Study Three. There is therefore some overlap between the methods for these two studies (particularly in terms of participant recruitment and selection criteria).

7.1 Study One: An EMA Study Examining the Moment-to-Moment Relationship Between PTSD Symptoms and Auditory Hallucinations in Daily Life.

7.1.1 Design

Study One employed a *micro-longitudinal* design using EMA (Mehl, Conner, & Csikszentmihaly, 2011); that is, EMA was used to examine the momentary relationships between the symptoms of interest in daily life, over a period of several days. EMA is a structured diary method in which participants are asked about various aspects of their symptoms and experiences at repeated time points in the course of daily life (Shiffman, Stone, & Hufford, 2008). Also frequently referred to as the *experience sampling method* or *ambulatory assessment*, EMA is increasingly used to study psychological processes involved in various mental health difficulties (Myin-Germeys et al., 2009). There is an increased recognition that, by nature, psychological theories of mental distress imply a dynamic relationship between psychological processes and symptoms of interest, and that EMA is an ideal method for capturing and testing these relationships. The use of real-time assessment of symptoms and experiences in the context of peoples' daily lives also has the benefit of reduced recall bias (Bradburn, Rips, & Shevell, 1987) and improved ecological validity (Myin-Germeys et al., 2009). There are a growing number of studies that have demonstrated the feasibility, acceptability, and validity of this approach in psychosis populations (Oorschot, Kwapil, Delespaul, & Myin-Germeys, 2009). EMA has successfully been used to examine the role of putative psychological processes in auditory hallucinations, including dissociation (Varese, Udachina, Myin-Germeys, Oorschot, & Bentall, 2011), worry and rumination (Hartley, Haddock, Vasconcelos, Emsley, & Barrowclough, 2014), and appraisals of power and control (Peters et al., 2012). Kimhy et al. (2017) showed that EMA assessments of hallucinations displayed

significant correlations with well-validated, semi-structured interviews that used typical retrospective reporting.

7.1.2 Inclusion and exclusion criteria rationale

Recruitment and data collection for Study One was partially nested within the protocol for Study Three (the pilot treatment study). Recruitment for these studies ran in parallel and participants taking part in Study Three provided baseline data (including a week of EMA monitoring) that was used in the analysis in Study One (n=14 who provided sufficient baseline data). In addition, a number of people were recruited to take part in Study One as a standalone study (n=16). Because of this overlap in recruitment, inclusion and exclusion criteria for Study One were aligned with the inclusion and exclusion criteria for Study Three. The rationale behind, and description of, inclusion and exclusion criteria for both studies is described in section 7.3.1.

7.1.3 The nature of EMA data

EMA produces a large volume of repeated measures data taken across a series of individual participants. As such, EMA data have a *multilevel structure* in which momentary measurements are nested within participants. Momentary level variables (captured by the EMA questions) are referred to as *level one* data, whereas participant level data (taken once during the study or aggregated into one value) lies at *level two* of the multilevel data structure. The nested nature of the data requires extensions to standard regression models, termed multilevel models. These models will be described further in Section 7.1.9.

7.1.4 Sample size rationale

Bolger and Laurencea (2013) outline eight factors that determine power to detect effects in intensive longitudinal studies that employ multilevel analyses: i) the

expected effect size for the average participant; ii) the sample size; iii) the number of measurement points for each participant; iv) the within-person variance in the predictor variables, v) the between-person variance in the effect; vi) the autocorrelation in error terms; vii) the within-person variance in the effect; and viii) the chosen alpha level. The fact that sources of variance occur both within and between participants makes power analysis for these multilevel studies complex. As a result, *rules of thumb* have most commonly been used to determine sample sizes in EMA studies in the field of psychological research. Kreft's '30/30' rule suggests that studies need to include 30 groups at level two (in the case of this study, 30 participants) with at least 30 measurements of the nested level one data (in this case 30 measurement time points). There has been some debate in the literature regarding this, however a review of simulation studies examining sample size and power in multilevel models concluded that the 30/30 rule is appropriate when the primary focus of the analysis is on level one effects (i.e. average effects across participants), as is the case in the current study (Hox, 2010b). Based on a 60% rate of compliance (as found in similar studies, e.g. Hartley, Haddock, Vasconcelos, Emsley, & Barrowclough, 2014) we expected to have 1080 data points to analyse across 30 people, thus meeting the '30/30' rule of thumb.

7.1.5 EMA item development

A central aspect of any EMA study is the items used to assess the constructs of interest. Items used in EMA questionnaires differ from those in standard retrospective, cross-sectional self-report measures in that they assess momentary experiences. Given that EMA has only recently gained traction as a method in mental health research, there are limited EMA items that have been previously validated (there are also issues with establishing reliability and validity that will be outlined in Section 7.1.5). There

has been a recent push to create an open access shared repository of EMA items that have been psychometrically validated (see https://osf.io/kg376/). In the absence of existing items, it is recommended that existing retrospective self-report measures can be used as a starting point, but that care should be taken to ensure that items assess momentary aspects of experience, rather than present-moment expressions of traits (Palmier-Claus et al., 2011). Other recommendations for item development include: using language that reflects how people describe their own behaviour and experiences, avoiding items that require extensive explanation, avoiding extreme or negatively worded items (which are likely to be less commonly endorsed), and ensuring that the total time to complete one questionnaire does not exceed two to three minutes (Kimhy, Myin-Germeys, Palmier-Claus, & Swendsen, 2012; Palmier-Claus et al., 2011). Finally, it has been suggested that experiences that are expected to be more frequent can be assessed in the moment with participants asked about their experiences *at the time of the signal*, whereas experiences that are less frequent can be assessed retrospectively with wording of the item asking about experiences *since the last signal* (Mehl et al., 2011). It is recommended that items regarding momentary experiences are asked first, followed by retrospective items (Kimhy et al., 2012).

The development of EMA items in the present study drew upon the above guidance. The items used are presented in Table 2. There have been a number of studies that have used EMA to assess auditory hallucinations in the flow of daily life. As such, the auditory hallucination item used in Study One was taken from a previous study and had previously been found to be acceptable and understandable within a psychosis population (Hartley et al., 2014). The item had also been found to show sufficient within-person variation to examine momentary associations with other psychological variables (Hartley et al., 2014). To be eligible for Study One

participants had to have persistent and frequent auditory hallucinations (occurring twice a week for at least six months). The requisite frequency of these experiences meant that a momentary assessment (i.e. 'Just before the beep…') was appropriate. The phenomenological features of auditory hallucinations also lend themselves to momentary assessment since they are commonly experienced as lasting for minutes or even hours at a time. Previous EMA studies using similar inclusion criteria have found hallucinations to be present on approximately 60% of occasions when assessed in the moment (Peters et al., 2012). In contrast, a literature search did not yield any appropriate EMA items for assessing momentary PTSD symptoms. The PTSD symptom items used in Study One were developed based upon common retrospective self-report measures for PTSD, and on DSM-5 PTSD symptom clusters, adapting items for brevity and to suit the shorter timeframe of the EMA schedule. Since our population were selected based on the presence of auditory hallucinations rather than the presence of PTSD per se, we predicted that PTSD symptoms would be less frequent and therefore less likely to be sufficiently captured using momentary assessments. In addition, the phenomenology of trauma memory intrusions is such that they are often experienced as very fleeting and momentary impressions, which would be less likely to be sufficiently captured by in the moment assessment. Symptoms of PTSD were therefore assessed retrospectively, using the wording 'Since the last beep…'. In line with recommendations, these items were delivered at the end of the questionnaire to reduce their influence on the momentary rating of auditory hallucinations (Kimhy et al., 2012). A decision was made not to assess all DSM-5 PTSD symptom clusters. Specifically, criterion D, *negative alterations in cognitions and mood,* was not assessed; the 'trait-like' characteristics of this construct make it more difficult to capture using momentary assessment. Also a large body of robust

EMA literature examining the role of negative affect in hallucinations (e.g. Myin-Germeys & van Os, 2007) already exists. All EMA items in this study were rated on a Likert scale from one to seven with one anchored to 'not at all', four anchored to 'moderately' and seven anchored to 'a lot'. This scale is the most widely used in similar EMA research (e.g. Hartley et al., 2014). It is worth noting that the auditory hallucination EMA item was measured using a one to seven Likert scale because this item was also used as an outcome measure of auditory hallucination severity in Study Three (thus data capturing the overall intensity of the experience was required). However, in line with the aims of Study One (to examine the predictors of momentary occurrences of auditory hallucinations), this item was dichotomised so that a score of 1 was coded as '0 = auditory hallucinations not present' and a score of 2-7 was coded as '1 = auditory hallucinations present'.

Table 2. EMA items used in Study One.

Construct	Item
Auditory hallucination intensity	**Just before the beep went off** I was hearing voices (that other people cannot hear)
Trauma-memory intrusion intensity	Thinking about the traumatic or stressful event(s) we identified as related to your voices…
	Since the last beep, memories of the event(s) came into my head when I did not want them to.
Posttraumatic avoidance intensity	Thinking about the traumatic or stressful event(s) we identified as related to your voices…
	Since the last beep I have tried hard to avoid thinking about or being reminded of the event (s).
Hyperarousal intensity	**Since the last beep** I have been constantly alert, on edge, irritable, or jumpy.

7.1.6 EMA sampling schedule

When designing an EMA study, various decisions need to be made regarding the sampling schedule (Kimhy et al., 2012; Palmier-Claus et al., 2011). Event-based sampling involves the assessment of experiences only following a predefined event. In the context of this study this would mean that participants would respond whenever they had an auditory hallucination. In contrast, time-based sampling involves assessment at random or fixed time points throughout the day. It has been recommended that time-based sampling is used when variables being measured are expected to occur relatively frequently (to reduce participant burden; Kimhy et al., 2012; Palmier-Claus et al., 2011). Participants in Study One were anticipated to have frequent auditory hallucinations, thus a time-based sampling design was deemed least burdensome. Also in line with recommendations, a random time sampling approach was chosen; participants were signalled to enter data at pseudorandom time points

throughout the day. This ensured a random sampling of experiences throughout the day and limited participants changing their behaviour in anticipation of a signal occurring (Kimhy et al., 2012). When determining the number of days and number of assessments per day in an EMA study it is important to weigh participant burden against gathering sufficient, representative data. A schedule of six days was chosen for Study One because this would inevitably span both weekdays and weekend days (providing a more global characterisation of experience). Ten assessment points per day were scheduled to provide sufficient level one data points (allowing for inevitable missing data (Kimhy et al., 2012). The sampling time was selected to be between 10am and 8pm each day, so as not to interrupt participants' sleep. The signals were pseudorandomised within one hour blocks, with at least 30-minutes between each signal (to reduce participant burden). To increase reliability of ratings, participants had to enter data within 15-minutes of the signal, otherwise the time point was considered to be missed. Previous EMA studies investigating auditory hallucinations have used a similar schedule and found good acceptability and compliance (Hartley et al., 2014; Varese et al., 2011; Peters et al., 2012).

7.1.7 EMA software

Historically, participants in EMA studies would use paper and pencil diaries and enter questionnaire information when signalled by an electronic beeper or pager. Contemporary EMA studies have made use of recent advances in digital technology and generally use smartphone-delivered assessments through mobile applications ('apps'). Participants are able to use their own smartphone or are provided with a study smartphone. The app is then downloaded onto the smartphone and the particular study schedule initiated. Data are uploaded to a secure server and downloaded by the researcher to be analysed in their statistical software package. One advantage of the

use of electronic data entry via smartphone apps is that data are time stamped, so researchers know exactly when each entry was completed. The MovisensXS app (https://xs.movisens.com) was chosen to deliver the EMA schedule in the present study, as this app was familiar to members of the study team who had used it in previous studies. MovisensXS offers a simple programming platform, provides technical support, and has a high level of security features to protect data. It was therefore deemed to be a suitable platform for the needs of this study. One drawback with the MovisensXS app is that it is only available on Android. This issue was managed by purchasing a number of Android smartphones that were lent to participants for the duration of the study. Figure 1. shows a participant view of the MovisensXS app presenting a study EMA item.

Figure 1. Participant view of the MovisensXS Smartphone App with the auditory hallucinations EMA item.
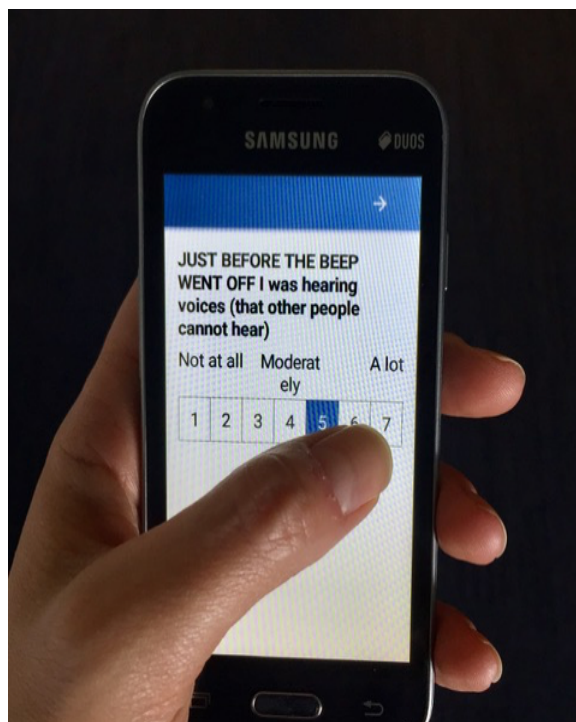
7.1.8 EMA item psychometrics

Establishing the psychometric properties of EMA scales and items is important to ensure that the data they produce is accurate and meaningful; however, assessing reliability and validity of new EMA items can be challenging. When exploring within-person associations it is required that items demonstrate a sufficient degree of variation at this level. Standard measures of test-retest reliability are therefore not appropriate given that changes over time are actually desirable. Additionally, it is recommended that the validity of EMA items should not be based purely on how well they correlate with other self-report or interview measures because these measures likely try to assess more global constructs averaged over time, rather than momentary states (Palmier-Claus, Haddock, & Varese, 2019). Additionally, assessing reliability and validity is more complex with multilevel data because variability exists at both the between- and within-person levels. Regardless of these challenges, there are some suggested methods of assessing the relevant psychometric properties of EMA items (Hektner, Schmidt, & Csikszentmihalyi, 2007) and these were used to assess the reliability and validity of the items used in Study One.

Within and between person variation

Mogle, Almeida, and Stawski (2015) outline the importance of estimating the between- and within-person variability. The focus of Study One is in exploring within-person associations; therefore it is important that items used demonstrate a sufficient amount of variation within each participant. Standard deviations of items were calculated at both the within- and between-person levels to examine within- and between-person variation. These values were calculated using the 'xtsum' command in STATA 14 and are shown in Table 3. All items showed within-person variation; however, across all items between-person variation was higher. This suggests that, the

items used had sufficient within-person variation, but there were likely to be important between-person differences in the intensity of auditory hallucinations.

Reliability

Hektner et al. (2007) outline an approach to examining the reliability of EMA items. Split-week reliability can be assessed by comparing aggregated responses in the first half of the sampling period with aggregated responses for the second half of the sampling period. The correlation coefficients between aggregate data from the first and second half of the sampling period in Study One are shown in Table 3. These suggest a high level of stability of aggregate ratings across the study, suggestive of appropriate reliability.

Table 3. EMA item means, standard Deviations (SDs) and split-week reliability.

Item	Mean	Within person SD	Between person SD	Split-week reliability (r)
AH occurrence (binary)	0.64	0.31	0.38	0.95
Trauma-memory intrusions	2.61	1.27	1.48	0.89
Avoidance	3.39	1.53	1.88	0.88
Hyperarousal	2.89	1.24	1.60	0.86

Validity

As per advice from Hektner et al. (2007), the validity of EMA items can be examined for convergent and discriminant validity with the other EMA items in the schedule. To be considered valid, associations between different items should show a pattern that is consistent with the theoretical construct of interest. Thus, items that we would expect to be related should show higher correlations (convergent validity) than those we would not expect to be related (discriminant validity; Hektner et al., 2007). Criterion validity can also be examined through comparison of aggregated EMA

scores with gold-standard retrospective measures that measure the same construct (Hektner et al., 2007). However, comparisons of EMA data with standard interview or self-report measures should be interpreted with caution, since when EMA measures and standard self-report measures diverge this may be more an indication of their different purposes (i.e. measuring momentary experiences versus retrospective summaries of an experience) than of a lack of validity (Hektner et al., 2007).

The EMA items in Study One were examined for convergent and divergent validity by calculating within- and between-person Pearson correlation coefficients. Within-person correlations were calculated as the correlation between level one EMA item ratings at each time point. Between-person correlations were calculated as the correlation of between individual participants' mean scores on each EMA item. Table 4 shows the Pearson correlation coefficient matrix, with between-person correlations shown as shaded values in the upper portion and within-person correlations shown in white in the lower portion. The between or within-person indicate that the constructs captured by the EMA items are related, but sufficiently distinct to consider them as independent constructs. Since the EMA items are all measuring different symptoms, this pattern supports the divergent validity of the items.

Table 4. Within- and between-person correlations (r) of EMA items.

Item	1	2	3	4
1. Auditory hallucination presence	1	0.54	0.54	0.62
2. Trauma-memory intrusion intensity	0.46	1	0.67	0.46
3. Avoidance	0.37	0.61	1	0.51
4. Hyperarousal	0.52	0.54	0.44	1

Note: Between-person correlations shown as shaded values and within-person correlations shown in white.

Measurement reactivity

A common concern with the use of frequent, daily measurements of symptoms and experiences is that repeated assessments may actually change the frequency or intensity of those variables (Kimhy et al., 2012). It has been recommended that studies that gather EMA data should assess for changes in EMA item responses over time as a check on reactivity effects that may affect the validity of the data (Myin-Germeys et al., 2018). As such, a series of hierarchical linear regressions were conducted in HLM 7 (Raudenbusch et al., 2011) with EMA items as the dependent variable and time point as the predictor variable. The results of these analyses are presented in Table 5. No significant associations were found between assessment time point and scores on any of the EMA items, suggesting that there was no measurement reactivity.

Table 5. Results of hierarchical regressions with EMA items as outcome variables and measurement time point as the predictor (*n*=28).

Variable	*B*	SE	*p*
Auditory hallucination presence	0.00	0.00	0.53
Trauma memory intrusions	0.00	0.00	0.77
Avoidance	0.01	0.01	0.25
Hyperarousal	0.01	0.00	0.19

Note, SE = standard error.

7.1.9 Analytic approach

Ecological momentary assessment data is rich and informative, however, the complexity that is inherent its structure presents unique challenges for analysis. This section will explore these issues and outline the approach taken for analysing data in Study One.

An overview of hierarchical linear models (HLM)

EMA methods produce intensive longitudinal data; a large volume of repeated measures data taken across a series of individual participants. As such, EMA data have a multilevel structure in which different measurement occasions are nested within individuals. Momentary level variables (captured by the EMA questions) are referred to as level one data, whereas other participant level data (taken once during the study or aggregated into one value) lies at level two of the multilevel data structure. As multiple measures are taken for each participant, the data are correlated such that two measurements from the same participant will be more similar to each other than two measurements taken from different participants. Approaches to the analysis of single level data, such as linear regression are based on the assumption that residual errors in the model are independent. The clustering inherent within EMA data violates this assumption of independence and different approaches to analysis are therefore required (Carter & Emsley, 2019). Additionally, although an EMA study is a repeated-measures design, standard analysis procedures such as repeated-measures analysis of variance (ANOVA) or multivariate analysis of variance (MANOVA) are also not recommended since these models cannot easily manage complexities in the data such as missing data, unequally spaced time points, and autocorrelated observations (Myin-Germeys et al., 2018).

Hierarchical linear models (HLM, also known as multilevel or random-effect models) are recommended for use in EMA research (Schwartz & Stone, 1998) and were utilised for the analysis of the data in Study One. The following description of HLM is drawn from various texts that provide a theoretical and technical overview of the use of these techniques (Black, Harel, & Matthews, 2012; Bolger & Laurenceau,

2013; Carter & Emsley, 2019; Hox, 2010a; Raudenbusch & Bryk, 2002; Schwartz & Stone, 1998).

Hierarchical linear models extend upon standard regression models by including additional random effects that can be used to account for person level differences in the model coefficients (intercepts and slopes). This type of modelling also allows within- and between-person relationships to be disaggregated. For example, the degree to which people with higher average levels of trauma-memory intrusions may also have higher average levels of auditory hallucinations (between-person) may differ from the degree to which momentary auditory hallucinations vary within a participant in relation to momentary trauma-memory intrusions (within-person). The HLM analysis can be conceptualised as a nested set of multiple regression equations. At level one, coefficients are estimated for effects on a dependent variable within each person. These estimates then become the dependent variables in the level two equations, in which estimates of overall effects are produced.

Hierarchical generalised linear models (HGLM) are an extension of HLMs that can estimate models for response variables that have error distributions that are non-normal. HGLMs using a Bernoulli distribution and logit link function are appropriate for dependent variables with a dichotomous outcome (Raudenbusch & Bryk, 2002).

Study One collected data that formed a two-level nested structure (EMA data points nested within participants) and had a dichotomous dependent variable, therefore the main effects analysis was conducted using two-level hierarchical generalised linear models (HGLM) with Bernoulli distribution and logit link function.

Moderator analyses in hierarchical models

Hierarchical models are well placed to understand cross-level interaction effects, that is, whether a level two variable (participant characteristic) is able to explain the variance in level one slopes. This is also described as a moderating effect. Secondary aims of Study One concerned the moderating effects of particular level two variables on the level one slopes; thus analyses of cross-level interactions were required. When there are a number of potential moderating variables of interest HLM-7 has functionality to conduct exploratory analyses to guide specification of the moderation models. These exploratory analyses involve a simple regression of the hypothesised level two moderating variables onto the residuals of the level one models. Where variables in this regression have an absolute t-value above two this indicates that they may be significant moderators. Thus, where hypothesised moderators had an absolute t-value above two they were entered as predictors of the level one model coefficients in the HGLM to test moderation hypotheses.

Analysis software

Hierarchical generalised linear models can be conducted using a variety of statistical software packages. HLM-7 (Raudenbusch et al., 2011) was chosen on the advice of a statistician (DM) who was involved in overseeing and checking the analysis. Given the candidate's lack of previous experience in using HGLMs, HLM-7 was considered an appropriate statistical software package because of its user-friendly interface and detailed instruction manuals. STATA 14 (StataCorp, 2015) was used to prepare the data and perform additional psychometric and person level analyses. STATA 14 has good data manipulation capabilities that were important for preparing the data for the HGLM.

Missing data

Missing data can be particularly prevalent in intensive longitudinal studies in which participants provide data at multiple time points. Hierarchical linear models are able to manage unbalanced data (in which different participants have different amounts of missing data); however, to reduce bias in the analysis it is still important to understand the mechanism of missingness in the data (Carter & Emsley, 2019). Missing data can be categorised as described by Little and Rubin (1987): missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR). MCAR occurs when the missingness of data is not associated with the observed or missing data. In this case the observed data can still be considered to be a random subset of the sample. However, in data that is MAR the missingness is related to the observed data in some way (but not the missing data). In this case the missingness can be occurring in a systematic way, but as long as the variables that predict missingness are measured and included in the model, unbiased estimates can be obtained (Black et al., 2012). Finally, data is considered MNAR if missingness is a function of the unobserved values themselves. Hierarchical linear models use maximum likelihood estimation, which benefits from being able to accommodate missing data, however an important assumption of maximum likelihood estimation is that the data are MAR. It is not possible to test whether data is MAR (since it is not possible to assess the influence of unobserved information). However, it has been suggested that this is a realistic assumption to make in a longitudinal data context, especially when assessment times are randomly chosen (Black et al., 2012; Carter & Emsley, 2019).

Observed values that may have been associated with missingness in Study One were examined in a series of simple linear regression analyses with the number

of missing waves (measurement occasions) as the dependent variable and i) EMA item means, ii) age, iii) gender, iv) CAPS-5 PTSD diagnosis, v) PSYRATS-AHS total score, and vi) diagnosis (psychotic/ not psychotic) as the predictors. The number of missing waves was square root transformed due to non-normality. Gender and CAPS-5 PTSD diagnosis were found to be significantly associated with the number of missing waves and were therefore explored and controlled for in all models as indicated (Black et al., 2012). Given the longitudinal nature of the data, it was also expected that noncompliance might increase over time due to fatigue effects. This was tested using a hierarchical generalised linear model (HGLM) with Bernoulli distribution and logit link function with wave missingness included as a dichotomous dependent variable and measurement occasion as the independent variable. There was a very small but significant increase in the likelihood of missing data over the course of the six days (OR = 1.01, $t - 2.73$, $p < 0.006$, 95% CI [1.00, 1.02]). As such, in line with advice by Bolger and Laurenceau (2013), the effects of time (measurement occasion and time of day) were explored and controlled for in all models when indicated.

Previous authors have suggested that the analysis of EMA data should only include participants who have completed at least one third of assessments (Delespaul, 1995). The statistical justification for this is unclear, however it has been posited that when people complete less than 33% of assessment points their data may not provide a representative sampling of their experiences. When analysing data for Study One this advice was weighed against the robustness of HLM in managing unbalanced data and the need for including a maximum number of data points to ensure statistical power. To maximise statistical power all participants were included in the main analyses. To check that this did not alter the significance or magnitude of the results

sensitivity analyses were conducted excluding any participants who completed less than one-third of assessment points (n=3). The sensitivity analyses conducted only on the sample that completed over 33% of the EMA assessment points (n=25) obtained the same pattern of results.

Assumptions of hierarchical models

Like any other statistical test HLMs and HGLMs have assumptions that must be met. Failure to meet these assumptions impacts upon the validity of the resulting models. Assumptions of HLMs are more complex to assess than those of simple regression models because assumptions apply at both levels and each level can have an impact upon the other levels in the model. Raudenbusch and Bryk (2002) outline six important assumptions of HLMs:

1) level one errors are independent, normal and homoscedastic;

2) level one predictors are independent of the model residuals;

3) random effects (level two errors) are independent, normal and homoscedastic;

4) level two errors are not related to level two predictors;

5) errors at level one and level two are independent;

6) and error terms at each level are independent of the predictors at the other level.

In contrast, HGLMs, as an extension of HLMs, have more relaxed assumptions. In particular, in line with the single level equivalent simple logistic regression models, HGLMs have relaxed assumptions regarding normality and heteroscedasticity of model residuals (Stoltzfus, 2011). There is limited literature available regarding diagnostic checks for model assumptions in HGLMs, so diagnostic checks for the HGLMs used in the Study One analysis were based upon the advice of a statistician (DM, a co-author in the peer reviewed publication of this

study). Firstly, HGLMs require that there is no collinearity between independent variables. The correlation matrix shown in Table 4 indicates that the independent variables used in Study One were only moderately correlated, suggesting collinearity was not an issue. In addition, to reduce potential issues with multicollinearity, level one data were person-mean centred. Person-mean centring (described in the 'model specification' section below) may lower correlations among model variables (Raudenbusch et al., 2011). Secondly, HGLMs require that there are no outliers that might influence the model coefficients. To assess for potentially influential outliers in Study One, the level two model variance (Maholonobis distance) was plotted against the expected chi square distribution. On visual inspection of these plots there were no participants who appeared to be model outliers.

Model specification

Model building took a bottom-up strategy, as recommended by Hox (2010a). Thus, model building began with a basic intercept only model (a null model in which the intercept is modelled as random and no predictors are included). Predictors and covariates (time variables and variables related to missingness) were then block entered with only the intercept random. In the final level one model, the model covariates with nonsignificant coefficients were removed and slopes for predictors were modelled as random effects where indicated by significant level two variance. Finally, level two interaction terms were entered into the model where indicated by the exploratory moderator analysis (described above).

When building HGLMs a number of decisions need to be made regarding the specification of the model. Decisions for the specification of models in Study One were made based on guidance in relevant texts regarding HLMs (Black et al., 2012;

Bolger & Laurenceau, 2013; Carter & Emsley, 2019; Hox, 2010a; Raudenbusch & Bryk, 2002; Schwartz & Stone, 1998).

Firstly, full-maximum-likelihood estimation was used for all HGLMs in Study One. It has been identified as an appropriate estimation procedure for intensive longitudinal designs because it can efficiently manage data that is unbalanced (where individuals may have differing numbers of observations spaced at different intervals; Black et al., 2012).

How predictors are centred is a critical aspect of hierarchical models. When predictors are entered into the model uncentred (using raw scores) model intercepts represent the expected outcome when the predictor equals zero. In cases (such as in Study One) where predictors are measured on scales in which zero is not a valid value, this is not appropriate. There are two different centring options that can be used to produce an interpretable intercept in these instances: grand-mean centring of predictor variables involves subtracting the sample mean of the predictor from each raw predictor score, whereas person-mean centring involves subtracting a person's mean score on the predictor from each raw predictor score provided by that person. Person-mean centring of level one variables is recommended when the primary substantive interest of a study involves data at this level (Raudenbusch & Bryk, 2002). Since the primary focus of Study One was characterising the average momentary within-person relationship between the predictors and the presence of auditory hallucinations, all level one variables were person-mean centred. Since zero is a valid value in dummy coded variables, dummy coded (dichotomous) variables were entered uncentred. Any level two predictors that were included in the models were entered grand-mean centred, since between-person differences were of primary interest for these variables.

One potential issue with EMA data is that of autocorrelation between data points. That is, data points that are temporally closer may be more correlated than those that are further apart. There are various ways to manage autocorrelation. Given the uneven spacing between data time points in Study One, the inclusion of the lagged (t–1) dependent variable was included in all models. Including the value for the dependent variable at the previous time point has been suggested as an appropriate way to reduce the influence of autocorrelation in time series data in which data points are not evenly spaced (Raudenbusch et al., 2011).

A key feature of intensive longitudinal data is the role that time may play in relationships between variables. Since all data points are strictly ordered in time, it is possible that time may be a confounding variable in relationships between predictors and dependent variables. For example, both the predictor and the dependent variable may vary according to the time of day, or the day of the week. Thus, any relationship between these variables may actually be a consequence of time, rather than a direct relationship between the variables. As suggested by Bolger and Laurenceau (2013) the effects of time (day of the week and time of day) were explored and controlled for in all models when indicated to reduce the confounding influence of time.

7.2 Study Two: A Meta-Analysis Examining Whether Trauma-Focused Therapies Delivered to Treat Comorbid PTSD in Psychosis Populations Have a Secondary Effect on Psychotic Symptoms.

7.2.1 Design

Study Two was a systematic review and meta-analysis of studies using trauma-focused therapies in psychosis populations. A meta-analysis is a statistical approach that allows the integration of evidence from multiple related studies. By extracting effect sizes and measures of variance from each study, a summary effect size can be

calculated. These summary effect sizes can then be used to summarise a research area, inform treatment and practice guidelines, or direct future research. A meta-analytic approach was suitable for Study Two since the aim was to estimate a quantitative effect of trauma-focused therapies on psychotic symptoms based on data available from a number of existing studies.

7.2.2 Preregistration of protocol

There are a number of decisions involved in conducting a meta-analysis that can have a large impact on the estimated effects calculated. For example, changes in inclusion and exclusion criteria, the selected outcomes of interest, and the type of analysis used can change the magnitude (or even the direction) of the pooled effects. Thus meta-analyses can be susceptible to researchers hypothesising after the results are known (HARKing; Kerr, 1998), or adjusting methods to achieve a desired result. Similarly, there may be a tendency to not publish nonsignificant results (Tricco et al., 2009). Preregistering protocols for meta-analyses can therefore reduce bias in results and publication bias because researchers have to declare their planned methods and outcomes in advance (Quintana, 2015). The PRISMA protocol (PRISMA-P) guidelines (Shamseer et al., 2015) provide a template for reporting meta-analysis protocols, recommending inclusion of details regarding: study rationale, study eligibility criteria, search strategy, moderator variables, risk of bias, and statistical approach. There are various online repositories for preregistering meta-analysis protocols. One of the most widely used is the International Prospective Register of Systematic Reviews (PROSPERO, https://www.crd.york.ac.uk/prospero/). In keeping with best practice for a robust and transparent meta-analysis, the protocol for Study Two was preregistered according to the PRISMA-P guidelines on the PROSPERO database (CRD42016035827).

7.2.3 Inclusion and exclusion criteria

As noted earlier, the inclusion and exclusion criteria of a systematic review and meta-analysis are crucial to establishing the scope of the empirical studies that will be included. Inclusion and exclusion criteria for Study Two were developed based on the aims of the study and the authors' pre-existing knowledge of the literature in the area. To be included in the review, studies had to: 1) be controlled or uncontrolled studies, providing quantitative data, 2) include participants with a diagnosis of a schizophrenia spectrum disorder or psychotic disorder, or selected on the basis of validated clinical measures of psychotic symptoms, and 3) assess the effectiveness of trauma-focused interventions with an evidence base for treating PTSD.

The treatment trial literature regarding the treatment of comorbid PTSD symptoms in psychosis is at a relatively early stage in its development; as such there are a number of uncontrolled studies and only a few randomised controlled studies. Therefore, with the aim of including as much data as possible in the estimation of effects, both uncontrolled and controlled studies were included. Separate analyses were then carried out for controlled and uncontrolled effects.

The majority of trials to date have included people based on a diagnosis of a schizophrenia spectrum disorder, however the symptom specific approach of this thesis informed a decision to additionally include trials that selected participants based on validated measures of psychotic symptoms. Although the main outcome of interest in this thesis is that of auditory hallucinations, we opted to include studies of general psychosis populations and to examine a range of psychotic outcomes. This was because prior knowledge of the literature indicated that there was limited research specifically in populations with auditory hallucinations and the majority of studies

focused on aggregated psychotic symptom outcomes, rather than symptom-specific auditory hallucination outcomes.

In keeping with the overall aims of the thesis the meta-analysis focused on the effects of psychological therapies that have demonstrated effectiveness for treating PTSD. Theory and research reviewed in Part I of the thesis has shown that PTSD symptoms may play a particular role in auditory hallucinations, thus the effects of treatments known to target these symptoms were of particular interest. The definition of psychological therapies with an evidence base for treating PTSD was based on the Australian Guidelines for the treatment of PTSD (Phoenix Australia, 2013); any psychological therapy that predominantly uses trauma-focused cognitive-behavioural techniques and including EMDR, PE, trauma-focused cognitive therapy, trauma-focused CBT, and cognitive processing therapy.

7.2.4 Search strategy

The search terms for the systematic review were based on authors' knowledge of the literature in the area, as well as key words identified by hand searches of important trials in the field. To capture a broad range of results, the search included key words within article titles and abstracts and used wildcards (i.e. asterisks) to capture minimal root terms (e.g. hallucinat*). In addition, Boolean search operators (AND, OR etc.) were used to focus and refine the results.

The search strategy involved the following key elements: 1) terms relating to schizophrenia spectrum or psychotic disorders, and 2) terms relating to trauma-focused psychological interventions. The precise search terms used were:

Psychosis OR psychotic OR psychoses OR schizophrenia OR schizoaffective OR

hallucinat* OR delusion* OR voices OR "hearing voices" OR "voice hearer" OR

bipolar OR "thought disorder" OR "severe mental illness"

AND

"Trauma focus*" OR trauma* OR PTSD OR "post traumatic" OR posttraumatic

AND

therapy OR psychotherapy OR psychological OR cognitive OR behavior* OR CBT

OR exposure OR reliving OR narrative OR rescripting OR "re-scripting" OR EMDR

OR "eye movement desensiti* reprocessing" OR treatment OR counsel*

Literature was searched from the inception of the databases until 25 March 2016 (the

date of the search). Articles were required to be in English, since there were not

sufficient project resources to allow for translation of non-English articles.

7.2.5 Selected outcomes

Although this thesis takes a symptom-specific focus, exploring the potential

effects of trauma-focused therapies on auditory hallucinations specifically, a decision

was made to examine a range of psychotic outcomes in the meta-analysis because

prior knowledge of the literature indicated that the majority of studies reported on

aggregated psychotic symptom outcomes, rather than symptom-specific auditory

hallucination outcomes.

Primary outcomes of interest in the final review were the severity of positive

and negative symptoms of psychosis, and specifically hallucinations and delusions

(where this information was available). Secondary outcomes of interest were PTSD,

depression and anxiety symptom severity. Initial preregistered outcomes of interest

did not include overall positive symptoms, however we included positive symptoms

as an additional outcome in the final analysis because it became apparent that this was

the outcome that most of the included studies reported on. This change from the

preregistered protocol is explained in the published manuscript in Chapter Nine. It is

common for meta-analyses to diverge from the preregistered plans and this is

considered to be acceptable practice as long as authors are transparent about this and

provide a rationale for any changes made (Quintana, 2015).

7.2.6 Assessment of risk of bias

Bias is systematic error or deviation from the truth in the results of a study

(Higgins & Green, 2011). Assessing the risk of bias in trials that are included in a

meta-analysis is important because variations in trial methodology and reporting can

lead to overestimations or underestimations of true treatment effects. For example,

trials that do not include blinding and allocation concealment frequently find inflated

effects. This has been demonstrated in the CBTp literature, in which trials that use

sufficient blinding and allocation concealment find much lower effects of CBTp than

those that do not (Jauhar et al., 2014). When synthesising studies in a meta-analysis a

full assessment of potential sources of bias can inform interpretations of the

robustness of pooled effect size estimates. There are a number of scales that provide

summary scores of risk of bias; however these have been criticised as lacking in

validity (Higgins & Green, 2011). The Cochrane collaboration recommend using their

risk of bias tool for the assessment of risk of bias in randomised controlled trials

included in systematic reviews and meta-analyses (Higgins & Green, 2011). The

Cochrane Collaboration tool rates each study as 'low', 'high', or 'unclear' risk for the

following criteria; 1) random sequence generation, 2) allocation sequence

concealment, 3) masking, 4) incomplete outcome data, and 5) selective reporting.

Studies that are rated as low risk of bias in all domains are given an overall rating of

low risk of bias, however if a study is rated as 'unclear' or 'high' on any domains then the overall rating is downgraded. This tool is designed for use in assessing randomised controlled trials but was chosen to rate all included trials in Study Two. This meant that uncontrolled studies automatically received a 'high risk' rating due to high-risk ratings on items 1-3. This was deemed to be a fair reflection of the risk of bias inherent in uncontrolled trials.

7.2.7 Analysis decisions

Study inclusion criteria meant that a number of case studies that included quantitative data were retrieved in the systematic review. It was not possible to synthesise these findings in the meta-analysis, so the findings were explored using narrative synthesis.

The meta-analytic synthesis of uncontrolled and controlled studies was conducted using Comprehensive Meta-Analysis 3.0. This software provides a user-friendly interface and comprehensive guidance in undertaking meta-analyses. Comprehensive Meta-analysis has various entry formats to estimate effect sizes for each study. Where possible, these effect sizes were calculated using means and standard deviations from the original study data. Where means and standard deviations were not available, effect sizes were calculated using other data provided in the original studies (for example from t statistics). The adjusted d (also known as Hedges' g) formula was used to calculate study effect sizes to adjust for the small sample sizes in many of the included studies. Pre to post treatment effect sizes were calculated using treatment change scores with standard deviations of change scores as the denominator (Lakens, 2013). Estimates of effect size in repeated measures data need to account for correlation in the measures. Since data was not available on the correlation between repeated measures in the original studies, a correlation of 0.70

was assumed, as suggested by Rosenthal (1991). Between-group effect sizes were calculated using post test means and pooled standard deviations.

The Comprehensive Meta-Analysis software synthesises effect sizes from the studies included in the analysis for each outcome into a summary effect. Weights are assigned to each study. Larger studies (that provide more precise effects) are assigned a larger weight than smaller studies (that have less precise effects). Researchers have to make a decision whether to use fixed-effects or random-effects models to synthesise the study effect sizes. A fixed-effects model assumes that the true effect size for all studies is identical (assuming that all studies included in the analysis are functionally identical (i.e. that subjects and interventions do not differ). In a fixed-effect model smaller studies are given a much smaller weight since it is assumed that there is much better information about the same effect size in the other studies. A random-effects model assumes that each study is providing information about a different effect size (because, for example, study populations or interventions differ) and the goal of the model is to estimate the mean of a distribution of effects. In a random-effects model small and large studies are assigned different weights, but the difference between weights is much smaller than that in a fixed-effects model. Random-effects models have larger confidence intervals than fixed-effects models because they include between-study variation. A decision to use random-effect models in Study Two was made a-priori, given the anticipated heterogeneity in included study interventions and designs.

7.3 Study Three: A Pilot Trial Assessing the Feasibility, Acceptability and Potential Effects of an Exposure-Based Trauma-Focused Therapy for Trauma-Related Auditory Hallucinations.

    7.3.1 Design

Study Three, the Recall study, was an uncontrolled pilot trial of a six session imaginal exposure intervention for trauma-related auditory hallucinations with outcome assessments conducted by an independent researcher at post treatment and one month follow up. The trial was prospectively registered as a pilot randomised-controlled trial, but a predetermined stop rule was implemented eight months into the trial due to slower recruitment than anticipated. At this point, the trial design (and registration) was amended to a smaller, uncontrolled trial.

        Pilot studies are generally scaled down versions of definitive trials that aim to assess whether components of the main study are acceptable and feasible, and to provide a preliminary assessment of the efficacy of the intervention (Lancaster, Dodd, & Williamson, 2004; Lee, Whitehead, Jacques, & Julious, 2014). This estimate of the effect of the intervention can determine whether a definitive trial is warranted, as well as informing the sample size calculation for such a definitive trial (Lancaster et al., 2004). The conception and design of the Recall study followed guidelines for pilot studies (Lancaster et al., 2004; Leon, Davis, & Kraemer, 2011), specifically aiming to assess the feasibility and acceptability of the overall trial design (the intervention, recruitment processes, eligibility criteria, assessments used etc.). The intervention being used was novel in this population and there were some indications that there might be feasibility and acceptability issues with the intervention itself (Gairns et al., 2015; Tong et al., 2017), therefore the trial had a primary focus on the feasibility and acceptability of the intervention specifically. Finally, the pilot study aimed to provide

preliminary estimates of intervention effects. A randomised-controlled design was initially deemed most appropriate to meet these aims since this would allow for testing of the feasibility of aspects of the trial design, including randomisation. It would also provide a more robust estimate of the effects of the therapy because of the use of a comparison control group.

The necessary change in the design of the study from a pilot randomised-controlled trial to an uncontrolled pre-post study had some potential implications for the scope of the results. Firstly, a pre-post study is more limited its ability to test the feasibility of the trial protocol for scaling up into a fully powered controlled trial, since it does not involve important aspects such as randomisation. Secondly, a pre-post study is likely to provide less robust estimates of the effects of the intervention, as uncontrolled trials tend to have inflated effect sizes. However, since the application of trauma-focused therapies for auditory hallucinations is a novel area of research, it was concluded that an uncontrolled study was still able to meet many of the aims of the pilot trial: exploring the feasibility and acceptability of aspects of the trial including recruitment rates and of the intervention itself, as well as providing an initial estimation of the effects of the therapy. It is important to note, that the low recruitment rate that led to the switch to an uncontrolled trial is important information regarding the feasibility of a future trial, and regarding the feasibility and acceptability of the intervention itself. This is discussed more in Chapter Twelve of this thesis.

7.3.2 Trial protocol registration

In recent years there has been growing concern that much psychological evidence is compromised by issues of selective reporting (when researchers conduct large numbers of different analyses using different combinations of variables and then

selectively report those that produce significant results) and publication bias (only publishing statistically significant results). This has led to increased emphasis on transparency in the conduct of psychological research (Nelson, Simmons, & Simonsohn, 2018). Similarly, there has been increasing recognition of publication bias in clinical trials in the broader field of biomedical research, with evidence that trials with positive findings are published more often, and more quickly, than trials with negative findings (Hopewell, Loudon, Clarke, Oxman, & Dickersin, 2009). Preregistration of research protocols is an important way of reducing problems with selective reporting and publication bias. Preregistration involves making key details about the design, conduct, and administration of planned studies available on a publicly accessible database before the study is conducted. This ensures transparency and accountability regarding planned outcomes and analyses and encourages publication of nonsignificant findings. Registering study protocols is recommended in psychological research (Klein et al., 2018) and clinical trials that contribute to evidence and guidance regarding treatments of health difficulties are now expected to be preregistered (National Health and Medical Research Council, 2018; World Medical Association, 2013). As such, to ensure transparency in the conduct and analysis of Study Three, the trial protocol was preregistered (ACTRN: 12616001503415) on the Australia and New Zealand Clinical Trial Registry (ANZCTR), the World Health Organisation endorsed registry for Australian clinical trials.

7.3.3 Inclusion and exclusion criteria

Identical eligibility criteria were utilised for Study One and Study Three. This was due to overlaps in participant recruitment and data collection in these two studies (data collection for Study One was partially nested within the procedures for Study

Three). Decisions regarding eligibility criteria for a study often involve weighing up a number of factors, including: the specific aims and questions of the research, external validity, feasibility, and ethical conduct. These issues will be explored with regard to key decisions made regarding inclusion and exclusion criteria for Study One and Study Three.

Firstly, participants were required to have current auditory hallucinations that were frequent and persistent (present for more than six months and occurring at least twice a week). To meet the aims of Study One and Study Three it was necessary to have a baseline level of auditory hallucinations that would enable detection of associations and potential change. Additionally, auditory hallucinations that have been present for less than six months are more likely to be fluctuating in their course and this would have limited detection of treatment effects. People with auditory hallucinations that had been present for more than six months were more likely to have a stable baseline of symptoms prior to treatment. An important point to note is that both studies focused on auditory hallucinations as a transdiagnostic phenomenon. Psychiatric diagnosis was not included in the eligibility criteria. As has been noted previously, auditory hallucinations are common across a number of different diagnostic categories and evidence suggests that there are no clear differences in the phenomenological characteristics of auditory hallucinations between people with different diagnoses (Larøi et al., 2012; Waters & Fernyhough, 2017). Additionally, it has been argued that symptom-specific, rather than diagnosis-based, approaches to psychological treatments for psychosis may improve efficacy, be more informative regarding specific mechanisms involved in auditory hallucinations, and may be more externally valid for clinical practice in which the reality is that people with distressing auditory hallucinations who seek treatment are likely to meet criteria for a range of

diagnoses (Thomas et al., 2014). Diagnostic categories also have questionable validity and utility in research that explores the underlying mechanisms and treatments for psychotic experiences (Bentall, 2014; Bentall, 1992). A transdiagnostic research strategy is also now reflected in the National Institute for Mental Health Research Domain Criteria (RDoC) approach which moves away from research based on diagnostic categories and focuses instead on basic dimensions of functioning (Ford et al., 2014).

Given that Study One and three were both concerned with posttraumatic psychological sequelae it was also necessary that participants had a history of traumatic events. The definition used for a 'traumatic event' was largely driven by research relating to the role of trauma in psychosis that has identified a broad range of traumatic and adverse experiences likely to be relevant. Based on this literature we chose to include PTSD criterion A traumatic events (experiencing or witnessing death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence), childhood adversity (physical, sexual or emotional abuse, or significant emotional or physical neglect), or significant bullying.

A key decision related to the definition of a 'trauma-related auditory hallucination'. The therapy delivered in Study Three involved exposure to the memory of a specific trauma deemed to be related to the person's auditory hallucinations. Additionally, to assess posttraumatic stress symptoms as a putative process of change, it was necessary to assess these symptoms in relation to this auditory hallucination-related index traumatic event. There is no clear consensus regarding what defines a trauma-related auditory hallucination. It has been suggested that similarities in content between auditory hallucinations and traumatic events may be a marker of a trauma-memory subtype of auditory hallucinations (McCarthy-Jones

et al., 2014), but content links are difficult to assess objectively (Hardy et al., 2005). Trauma-informed cognitive behavioural models of auditory hallucinations also indicate that traumatic sequelae may also be involved in auditory hallucinations that do not have clear content links with the traumatic event (Hardy, 2017). Given the lack of consensus in characterising auditory hallucinations that may be trauma-related and the early stage of this research, we opted to include people based on their own subjective understanding of links between their auditory hallucinations and their trauma history. This also meant that people entering the study were able to identify a relevant index trauma memory to work on in therapy and were motivated to undertake a trauma-focused therapy. In Study Three we were specifically interested in assessing the effects of the exposure component of the therapy (postulated to act most potently on the mechanisms of interest) rather than broader trauma-focused approaches that might involve more substantial time spent on formulation of trauma-auditory hallucination links and developing a rationale for using a trauma-focused approach. To feasibly deliver and evaluate brief standard-protocol imaginal exposure it was therefore a necessary prerequisite that participants came to therapy with a relevant index trauma memory to work on in therapy and already had established a rationale for undertaking this sort of therapy work.

A final important consideration in establishing the eligibility criteria for Studies One and Three pertained to issues of risk. Evidence has generally indicated that trauma-focused therapies are safe and do not lead to symptom exacerbation in psychosis populations (van den Berg et al., 2015a, 2015b), however other research has indicated that distress and symptom exacerbation may be important to consider (Tong et al., 2017). It was decided that objective risk criteria (based on standardised interview schedules in the baseline assessment) would be set at a relatively high

threshold (acute risk to self or others, defined by the presence of suicidal or homicidal thoughts with current intent, similar to the criteria of (de Bont et al., 2013). In addition, it was deemed necessary to balance this with the opinions of the participant's treating team who would be more able to provide a nuanced assessment of the risk that doing a trauma-focused therapy might pose, thus a further exclusion criteria was that the participant's treating team reported that undertaking the study treatment would pose a serious risk to the safety of the participant or other people.

7.3.4 Selecting the intervention

There are a number of evidence-based psychological therapies for PTSD (Bisson et al., 2007). Postulated psychological mechanisms of primary interest in Study Three were trauma-memory intrusions and the nature of the trauma memory. It was important that the intervention used in Study Three was an intervention known to act on these mechanisms. Imaginal exposure from the PE protocol was chosen for several reasons. Firstly, PE has the most robust evidence base for treating PTSD (and thus reducing trauma-memory intrusions). Secondly, exposure to the trauma memory has been implicated as a crucial intervention component when treating posttraumatic stress symptoms in psychosis populations (Hardy & van den Berg, 2017). Thirdly, giving a verbal narrative of the trauma memory (the vehicle of exposure in imaginal exposure) is hypothesised to act on the nature of the trauma memory, through elaborating and contextualising it (Hackmann et al., 2004; Speckens, Ehlers, Hackmann, & Clark, 2006). Standard protocol PE had also been trialled in the largest study of trauma-focused therapy for PTSD in a psychosis population, with findings suggesting that it was feasible and safe to deliver in its standard from in this population (van den Berg et al., 2015b).

7.3.5 Choice of clinical outcome measure

A crucial methodological decision in any treatment trial is the selection of an appropriate primary outcome and a suitably reliable and valid way to measure this outcome. As a pilot study the primary aims of Study Three related to feasibility and acceptability, however primary and secondary clinical outcomes were also assessed to provide estimations of the effects of the intervention. The primary outcome was chosen based on the intervention target. The intervention specifically aimed to target auditory hallucinations so a measure of the overall severity of auditory hallucinations was considered an appropriate primary effectiveness outcome. The PSYRATS-AHS (Haddock, McCarron, Tarrier, & Faragher, 1999) has been widely used in psychological therapy trials for psychosis and captures a range of important dimensions of auditory hallucination severity, including distress, frequency, attribution and loudness (Woodward et al., 2014). Previous psychological therapy trials for auditory hallucinations have used subscales or specific items of the PSYRATS-AHS to measure change in specific dimensions of auditory hallucinations considered relevant to the therapy mechanisms. For example, the COMMAND trial separated distress and negative content items (Birchwood et al., 2014) and a trial of relating therapy for auditory hallucinations used the distress subscale (Hayward et al., 2017). Since the imaginal exposure intervention aimed to target a putative causal mechanism in trauma-related auditory hallucinations, it could be hypothesised that the frequency of auditory hallucinations would reduce. However, theoretical models regarding the role of posttraumatic processes in auditory hallucinations would also indicate that auditory hallucination content or distress might change (Hardy, 2017). Given the early stage of the research and lack of knowledge about the potential mechanisms of change in imaginal exposure for auditory hallucinations, it was

deemed appropriate to measure overall auditory hallucination severity using the total PSYRATS-AHS score.

In addition to the PSYRATS-AHS we chose to include EMA measures of auditory hallucination intensity and distress as another measure of the primary outcome (auditory hallucination severity). This was because of concerns about the sensitivity of the PSYRATS-AHS. For example, the PSYRATS-AHS measures the frequency of auditory hallucinations on a 4-point scale: 0 = Voices not present or present less than once a week, 1 =Voices occur for at least once a week, 2 = Voices occur at least once a day, 3 = Voices occur at least once an hour, and 4 =Voices occur continuously. Thus, for example, the PSYRATS-AHS would not detect a change in the frequency of auditory hallucinations from five times each week to once a week. This would potentially be clinically significant change but would not be captured. Although not yet widely used as an outcome tool in psychological treatment trials, EMA has been suggested to provide a more sensitive measure of symptom outcomes for clinical trials, subject to less retrospective bias (Verhagen, Hasmi, Drukker, van Os, & Delespaul, 2016). EMA measures of auditory hallucination intensity and distress were therefore chosen as measures of change that were potentially more sensitive. The EMA items used in Study Three are described in the peer-reviewed manuscript for this study (Chapter Eight).

Secondary effectiveness outcomes for Study Three were chosen to reflect other symptoms that might be expected to change as a result of a trauma-focused therapy in this population – PTSD symptoms, delusions, depression and anxiety.

7.3.6 Choice of process measures

Theory and research have highlighted a number of psychological processes that might be involved in trauma-related auditory hallucinations. Imaginal exposure

was selected as the intervention for Study Three based on previous evidence of its effects on trauma-memory intrusions and trauma-memory processing (both implicated in trauma-informed theories of AH (Fowler et al., 2006; Hardy, 2017; Steel et al., 2005). Thus, it was important to estimate whether the imaginal exposure intervention in the context of Study Three did act on these postulated mechanisms of action.

EMA was chosen as a measure of trauma-memory intrusion intensity and distress and there is a discussion of the development of these items in Section 7.1.4 and in the peer-reviewed publication in Chapter Ten.

Measures of trauma-memory processing in the PTSD literature have generally used two methods: self-report scales and ratings of trauma narratives. Studies have used self-report scales aiming to capture aspects of memories that are thought to be a result of a data-driven processing style (disorganisation of the memory, intrusiveness of the memory, sensory detail in the memory etc.). However, the field is lacking a well-validated measure that has been used consistently. Measures of data-driven processing have also shown significant correlations with other constructs such as peri-traumatic dissociation and self-referent processing, making it difficult to parse the specific role of different aspects of information processing during traumatic events.

Another method that has been used to assess the nature of trauma memories is objective coding of specific features of trauma narratives (thought to provide a proxy measure of the nature of the memory). A recent review noted some heterogeneity in the results of research examining the nature of trauma narratives in relation to PTSD, but found robust evidence for trauma narratives in people with PTSD being dominated by sensory, perceptual and emotional details, which can be considered to be indicative of a data-driven processing style (Crespo & Fernandez-Lansac, 2016).

Based on this literature, two assessments of the nature of the trauma memory were used in Study Three. Firstly, the Trauma Memory Questionnaire, a self-report measure that has been validated in a PTSD population (Halligan et al., 2003) was included. Secondly, a programme called Linguistic Inquiry and Word Count (Pennebaker, Boyd, Jordan, & Blackurn, 2015) was used to analyse participant trauma narratives. Linguistic Inquiry and Word Count is a widely used tool for computerised text analysis that processes written text and classifies words into various dimensions. The output provides information on the percentage of words in the text that fall into specified classifications. To provide an assessment of the extent to which memories were encoded in a sensory-perceptual or a semantic (cognitive) form, LIWC was used to calculate the percentage of words classified as 'perceptual' (e.g., see, hear) and 'cognitive' (e.g. cause, maybe, know) processes.

7.3.7 Analysis decisions

Omitting statistical significance testing

There is some debate regarding the use of tests of statistical significance in pilot trials. It is argued that pilot trials are more about exploration than confirmation (Lee et al., 2014) and pilot trials are also generally underpowered to achieve statistical significance at the commonly used 5% threshold (Lancaster et al., 2004). Recommendations suggest that the focus of pilot trials should be on descriptive statistics and estimation, rather than significance testing (Lancaster et al., 2004; Lee et al., 2014; Leon et al., 2011). Despite these recommendations, the majority of trials have continued to use hypothesis testing with assessments of statistical significance (Arain, Campbell, Cooper, & Lancaster, 2010). Based on guidance and current standard practice in the field, a decision was made to focus the analysis of Study Three on estimates of effect size and confidence intervals, and to include significance

tests as a secondary analysis. This was a preregistered analysis, but at the analysis stage our sample size was smaller than anticipated. This weakened the argument for statistical significance testing even further (given even lower power to detect an effect). A decision was made to omit statistical significance testing from the analysis. This deviation from the preregistered analysis was justified in the peer-reviewed journal article (Chapter Ten) to ensure transparency.

Managing missing data

There were two different types of missing data that needed to be managed prior to the data analysis for Study Three. Firstly, there was a small number (<5%) of individual items missing within individual assessment measures (item nonresponse). Little's MCAR test was used to determine whether there were patterns within the missing values that indicted nonignorable missing data. This test was not significant ($p > 0.5$), suggesting that the missing data was MCAR. It was therefore decided that estimation-maximisation (EM) using IBM SPSS Statistics Version 25 would be appropriate for imputing these missing values.

The second type of missing data was from the three participants who did not complete their post treatment or one month follow up assessments. Given that it was unlikely that this data was MAR (i.e. the reason for noncompletion was likely to be related to unobserved values – potentially that these participants had increased symptom severity scores) and the small sample size, imputation methods were not considered to be appropriate. Listwise deletion was used for data analysis, meaning that the analysis was only based on the data of the participants who completed all of the follow up assessments (termed an *available-case analysis*; Higgins & Green, 2011)

Measures of effect sizes

Effect sizes are standardised measures of the difference between two values. Cohen's d is a widely used effect size measure that expresses a difference score as a number of standard deviations. Effect sizes like Cohen's d have the advantage of helping to quantify the size of an effect. An additional benefit is that Cohen's d can provide information that is comparable across different studies, even when different measures have been used (Cumming, 2011). Effect sizes can also be used to provide information to design future studies, since the size of the effect informs the necessary sample size in an a priori power analysis (Lakens, 2013). Cohen (1988) set out benchmarks for interpreting effect sizes, where d = 0.2 is small effect, d = 0.5 is a medium effect, and d = 0.8 is a large effect. However, it is also recommended that the practical consequences of the effect should be considered when interpreting its importance (Cumming, 2011; Lakens, 2013). There are a number of ways to calculate Cohen's d and differences depend upon the standardiser used. In a repeated measures design (like that used in Study Three) there are three main standardiser options – the standard deviation of the mean difference, the pooled standard deviation of the pre and post test means, or the standard deviation of the pre test mean. When an experimental manipulation occurs between the pre test and post test assessment and there is good reason to believe that this may affect the standard deviation, it is recommended that the appropriate standardiser for Cohen's d is the pre test standard deviation (Cumming, 2011; Lakens, 2013). In Study Three, we anticipated that the intervention would increase variability in participants' symptom measures (since some people were likely to respond more than others). We therefore used the pre test standard deviation as the standardiser. Thus the formula used to calculate Cohen's d in Study Three was:

$$d = \frac{M^{1-}M^2}{SD_{pre}}$$

This formula for Cohen's d gives a biased estimate of the population effect size, particularly for a small sample. Thus, it is recommended that Cohen's d is corrected to unbiased d (also known as Hedge's g; Cumming, 2011). The formula for unbiased d is:

$$d_{unbiased} = Cohen's\ d\ \times \left(\frac{n-3}{n-2.25}\right) \times \sqrt{\frac{n-2}{n}}$$

Effect sizes and confidence intervals around the mean difference were calculated using the Exploratory Software for Confidence Intervals (ESCI; Cumming, 2011).

Managing non-normal data

Histograms, Q-Q plots, and the Shapiro-Wilk test were used to inspect the data for normality prior to conducting descriptive statistics and the estimation of effect sizes and confidence intervals. Additionally, boxplots were used to identify any univariate outliers.

There were no problematic outliers identified; however, the PSYRATS-Delusions subscale and the perceptual detail in the trauma narrative variables were not normally distributed. Since the mean can be affected by skewed data, the median and interquartile range were reported for these variables. The median change was calculated as median of the change scores. As suggested by Rosenthal (1994), effect size *r* was calculated from the Wilcoxon signed rank z using the formula:

$$r = \frac{z}{\sqrt{n}}$$

This was then transformed into unbiased d to ensure it was comparable with the effect sizes for other variables. Standard calculations of 95% confidence intervals and effect

sizes are also based upon assumptions of normality (Cumming, 2011), therefore nonparametric calculations for effect size and confidence interval were used for these variables. Confidence intervals around the median change score were calculated according to (Campbell & Gardner, 1988), where the lower 95th confidence limit is given by the:

$$\frac{n}{2} - \frac{1.96\sqrt{n}}{2} \; th \; ranked \; value$$

and the upper 95th confidence interval is given by the

$$1 + \frac{n}{2} + \frac{1.96\sqrt{n}}{2} \; th \; ranked \; value$$

7.4 Additional features of the current research

7.4.1 Involvement of people with lived experience

There has been an increasing international emphasis on involving people with lived experience in all stages of the research process. *Lived experience involvement* refers to the active engagement of people with experience of using mental health services and/or mental health difficulties in planning, undertaking, and disseminating research.

Experts by lived experience are able to bring unique skills to the research process since they are able to offer different perspectives based on their own experience of the topics under investigation. The unique perspectives and skills of people with lived experience can therefore complement the skills that researchers without lived experience are able to bring to the research process. There are many recognised benefits in involving people with lived experience as partners in the research process, including benefits for the relevance, robustness and participation rate of the research itself (Ennis & Wykes, 2013; Staley, 2009), as well as wider

benefits in empowerment and social justice for the people that the research outcomes are most relevant to (Tait & Lester, 2005).

Within Australia, the increased recognition of the value of lived experience involvement in research has been reflected in the National Health and Medical Research Council statement on consumer and community participation in health and medical research (2004) and in the consideration of lived experience involvement being incorporated into the review process for many research funding bodies.

The candidate led a project to secure funding for, and develop a lived experience advisory panel to inform the work of the supervisor's lab group. This panel of five people meet regularly to consult on projects being conducted in the lab. The studies that make up this thesis were discussed with the panel and their feedback has been incorporated into aspects of the design and reporting of these studies. Specific areas that the lived experience panel were consulted on were the EMA items used, ways to improve the feasibility of a future trial, ways the therapy might be adapted in future, and general implications of the findings.

7.4.2 Funding

The programme of research undertaken in this thesis was supported by an AUD $4100 grant from the Barbara Dicker Brain Sciences Foundation in October 2016. This grant was used to support participant reimbursements.

Chapter Eight: Moment-to-Moment Associations Between Posttraumatic Stress Symptoms and Auditory Hallucinations in the Flow of Daily Life (Publication Two).

8.1 Preamble to Publication Two

Publication Two outlines the rationale, methods, and findings of Study One, an EMA study examining associations between PTSD symptoms and auditory hallucinations in daily life. This study aimed to move beyond previous research in this area, which had been predominantly cross-sectional, to explore the dynamic moment-to-moment relationships implicated in trauma-informed cognitive behavioural theories of trauma-related auditory hallucinations (Hardy, 2017; Steel et al., 2005).

Publication Two has been submitted and is currently under review for publication. The 'Author Indication Form', which details the nature and extent of the candidate and co-authors' contributions to this manuscript is included in Appendix IV. The results of this study were also presented as an open paper at the World Congress for Behavioural and Cognitive Therapy (WCBCT) in Berlin in July 2019 and in a Swinburne University Centre for Mental Health research symposium in August, 2019. The complete citations are as follows:

Brand, R.M., Bendall, S., Hardy, A., Rossell, S.L., Meyer, D., and Thomas, N. (under review). Moment-to-moment associations between posttraumatic stress symptoms and auditory hallucinations in the flow of daily life.

Brand, R.M., Bendall, S., Hardy, A., Rossell, S.L., Meyer, D., and Thomas, N. (2019). Moment-to-moment associations between posttraumatic stress symptoms and auditory hallucinations in the flow of daily life. Open paper presentation at the World

Congress for Behavioural and Cognitive Therapies (WCBCT) conference, Berlin, Germany.

Brand, R.M., Bendall, S., Hardy, A., Rossell, S.L., Meyer, D., and Thomas, N. (2019). Moment-to-moment associations between posttraumatic stress symptoms and auditory hallucinations in the flow of daily life. Open paper presentation at the Swinburne University Centre for Mental Health annual research symposium, Melbourne, Australia.

8.2 Abstract

Traumatic events are associated with increased risk of auditory hallucinations and posttraumatic stress symptoms have been implicated in this relationship. We aimed to explore the moment-to-moment relationship between posttraumatic stress symptoms and auditory hallucinations in daily-life. Twenty-eight people with persistent auditory hallucinations and a history of traumatic events completed six days of ecological momentary assessment. We assessed auditory hallucinations, trauma memory intrusions, avoidance, and hyperarousal at 10 time points each day. Multilevel modelling showed that the severity of trauma memory intrusions (but not avoidance or hyperarousal) within the preceding hour was associated with the occurrence of auditory hallucinations. This relationship was significantly stronger for people with a direct link between the content of their auditory hallucinations and trauma history. In time-lagged analyses, main effects of trauma memory intrusions, avoidance, and hyperarousal on auditory hallucinations were not significant. Trauma memory intrusions have momentary associations with auditory hallucinations and this relationship is stronger and more enduring for those with a direct link between their

auditory hallucinations and the trauma. Our findings are in keeping with the proposal that intrusive trauma memories are associated with the occurrence of (some) auditory hallucinations.

Key words: hallucinations; trauma; intrusions; posttraumatic stress disorder; ecological momentary assessment.

8.3 Highlights

- Traumatic life events are associated with increased risk of auditory hallucinations and it has been suggested that posttraumatic stress symptoms (trauma memory intrusions, hyperarousal and avoidance) are involved in this relationship.

- This study shows that trauma memory intrusions are associated with the occurrence of auditory hallucinations in day-to-day life, supporting the idea that some auditory hallucinations are shaped by trauma memory intrusions.

8.4. Introduction

Auditory hallucinations[1] are reported by people with a range of psychiatric diagnoses, including schizophrenia spectrum disorders, mood disorders, borderline personality disorder, and posttraumatic stress disorder (Larøi et al., 2012). A substantial proportion of people who have auditory hallucinations have experienced trauma (Daalman et al., 2012) and there is mounting evidence that traumatic events play a causal role in the development of psychotic experiences (Kelleher et al., 2013;

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[1] For the purposes of this manuscript we use the term 'auditory hallucinations' to refer to a range of auditory experiences that can occur in the absence of corresponding external stimuli. However, we note that many people may prefer different terms to describe their experiences, such as 'voices', 'voice-hearing', or 'hearing voices'.

Varese, et al., 2012). Understanding the psychological mechanisms involved in this relationship will inform the development of therapies for auditory hallucinations.

Theoretical models and research studies have implicated a range of posttraumatic processes in the relationship between trauma and psychotic experiences. These include posttraumatic stress symptoms (trauma memory intrusions, avoidance and hyperarousal; Williams et al., 2018), which are prevalent in people with auditory hallucinations (de Bont et al., 2015) and are significantly associated with auditory hallucinations in trauma-affected populations (Alsawy et al., 2015).

Trauma memory intrusions are of particular interest due to their phenomenological similarities with auditory hallucinations: both are experienced as involuntary sensory-perceptual intrusions, and often represent a current threat (Morrison et al., 2003). The content of auditory hallucinations often relates to the content and themes of traumatic experiences (Hardy et al., 2005), much like intrusions of traumatic memory content. Trauma-informed models of auditory hallucinations have drawn on cognitive-behavioural theories of PTSD to understand the role of trauma memory intrusions in auditory hallucinations. Specifically, contemporary theories of PTSD outline that poorly contextualised sensory information is prone to involuntary recall (i.e. trauma memory intrusions) because of disruptions to information processing during the traumatic event (Brewin, 2015; Ehlers & Clark, 2000). A more severe form of this process may lead to auditory hallucinations, which have been conceptualised as extremely fragmented and decontextualised trauma memories (Hardy, 2017; Steel et al., 2005). Trauma memory intrusions mediate the relationship between childhood trauma and auditory hallucinations (Peach et al., 2018) and cognitive processing styles implicated in trauma memory intrusions do

increase the likelihood of hallucinatory experiences following traumatic events (Geddes et al., 2016).

Posttraumatic avoidance and hyperarousal have also been implicated in cognitive-behavioural theories of auditory hallucinations, and are conceptualised as emotional regulation strategies, or attempts to manage threat (Dodgson & Gordon, 2009; Hardy, 2017; Morrison et al., 2003). Posttraumatic avoidance may directly increase trauma memory intrusions through rebound effects and contribute to vulnerability to memory intrusions by hindering the cognitive processing of trauma memories (Morrison et al., 2003). Hyperarousal (including hypervigilance) increases attention to threatening stimuli and may increase the chance of 'false positives' in detecting threat in environmental noise, potentially leading to auditory hallucinations (Dodgson & Gordon, 2009). In support of these theories, posttraumatic avoidance and hyperarousal have been found to mediate the relationship between trauma and auditory hallucinations (Hardy et al., 2016; Powers et al., 2016).

To date, support for the role of posttraumatic stress symptoms in auditory hallucinations has been largely cross-sectional. As such, the dynamic relationship between posttraumatic stress symptoms and auditory hallucinations remains unclear. Ecological momentary assessment (EMA), involving the collection of data from an individual over repeated measurements, in the context of daily life, can more clearly capture this dynamic relationship. If decontextualised trauma memory intrusions play a role in the occurrence of auditory hallucinations, then we would expect that they would be more likely to occur in the context of, or following, episodes of trauma memory intrusions. Similarly, if posttraumatic avoidance and hyperarousal play a role, then we would expect that auditory hallucinations are more likely in the context of, or following, them. Ecological momentary assessment has successfully been used to

examine the role of other psychological processes in auditory hallucinations (Hartley et al., 2014; Peters et al., 2012; Varese et al., 2011).

Mechanisms involved in auditory hallucinations are likely to vary from person-to-person (McCarthy-Jones et al., 2014) and trauma-related psychological processes may only be relevant for a subgroup of people (Luhrmann et al., 2019). It is not yet clear how to identify this trauma-related auditory hallucination subgroup, but theory and literature would indicate that content links between trauma and auditory hallucinations (Hardy, 2017; Hardy et al., 2005), the nature of trauma memory processing (Steel et al., 2005), and levels of PTSD symptoms (Morrison et al., 2003) may be important. Understanding between-person moderators of the momentary relationship between posttraumatic stress symptoms and auditory hallucinations will help to identify those for whom posttraumatic stress mechanisms are of most relevance and thus target future interventions more effectively.

8.5 Aims

We aimed to examine moment-to-moment associations between posttraumatic stress symptoms and auditory hallucinations using EMA. We hypothesised that trauma memory intrusions, avoidance, and hyperarousal would be associated with the occurrence of auditory hallucinations and examined both proximal (occurring within the preceding time period) and lagged (occurring in the previous time period) effects. We also aimed to explore between-person moderators, specifically hypothesising a stronger relationship for people with auditory hallucination content directly related to their trauma history, people with more disorganised and intrusive trauma memories, and people meeting criteria for PTSD.

8.6. Methods

8.6.1 Participants

We invited people attending a specialist psychological therapy clinic for people experiencing auditory hallucinations and people on an auditory hallucination research participant registry to take part. We also promoted the study in local mental health services. Participants were required to (a) be aged 18-75; (b) have auditory hallucinations (confirmed using item K6b of the MINI 7.02, Psychotic Disorders version, Sheehan et al., 1998) that were frequent and persistent (present for more than six months, occurring at least twice a week); (c) report a history of criterion A traumatic events, childhood adversity or significant bullying; and (d) have a sufficient level of English language to participate. Potential participants were excluded if they had substance induced auditory hallucinations or current substance dependence issues (assessed using the MINI 7.02) that would interfere with participation or an estimated IQ<70 using the Wechsler Test of Adult Reading (Wechsler, 2001). These selection criteria are identical to those used for an adjoined treatment study. In line with requirements for the treatment study, participants had to have made some conceptual links between their past adverse experiences and their auditory hallucinations.

8.6.2 Procedure and measures

Baseline assessment (pre-EMA).

Demographic information.

We used a self-report questionnaire to collect demographic information including; age, gender, ethnicity, highest level of education, current psychiatric medication, and duration of auditory hallucinations.

Psychiatric diagnosis.

Psychotic disorder diagnoses were confirmed using the MINI 7.02, Psychotic Disorders version (Sheehan et al., 1998). We assessed for borderline personality disorder using the borderline personality disorder scale of the Structured Clinical Interview for DSM 5 (SCID 5; First, Gibbon, Spitzer, & Williams, 1997) and PTSD diagnosis using the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Weathers et al., 2013a).

Auditory hallucination severity.

We used the Psychotic Symptom Rating Scales Auditory Hallucinations Scale (PSYRATS-AHS; Haddock et al., 1999) as a measure of auditory hallucination severity. The PSYRATS is an interviewer administered, multidimensional measure of auditory hallucinations.

Trauma history.

Trauma checklists were used to ascertain eligibility and determine the extent and nature of trauma history. DSM-5 PSTD diagnostic criterion A events were assessed using the Life Events Checklist for DSM-5 (LEC-5; Weathers et al., 2013b). Experiences of childhood abuse and neglect were assessed using the Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998). A single item taken from the trauma history questionnaire (Hooper, Stockton, Krupnick, & Green, 2011) assessed bullying.

Disorganisation and intrusiveness of the trauma memory.

The nature of the participant's memory of the traumatic event was assessed using the Trauma Memory Questionnaire (TMQ; Halligan et al., 2003). The TMQ assesses aspects of traumatic memories that are hypothesised to result in intrusive re-experiencing. A 5-item disorganisation subscale assesses deficits in intentional recall

and an 8-item intrusiveness subscale assesses a wider range of phenomenological characteristics such as the associated emotion and reliving, vividness and 'nowness' of the memory.

Voice-trauma content link.

Participants reported up to three examples of the most distressing auditory hallucination content over the last week as part of their PSYRATS interview, and details of the traumatic event as part of the CAPS-5 interview. The descriptions were rated using criteria adapted from Hardy et al. (2005). Specifically, we rated whether participants had a direct relationship between their trauma content and auditory hallucination content (operationalized as auditory hallucination content including a literal correspondence to trauma content, i.e. exact words, phrases or sounds heard at the time of the trauma). These ratings were made at the conclusion of the initial interview, prior to EMA data collection (concordance between two independent raters was 100%).

EMA.

Participants were provided with an Android smartphone with the MovisensXS app (https://xs.movisens.com) installed and the study schedule preloaded. Participants were trained to use the app and given a practice block of questions to ensure they understood the procedure. The EMA assessment period started immediately following the baseline assessment.

Participants completed six days of monitoring using a time-based schedule of 10 assessments per day between the hours of 10am and 8pm with stratified pseudorandom sampling (assessments occurred at random within one hour time blocks, with a minimum of 30 minutes between each assessment). Assessments not completed within 15 minutes of the signal were logged as missed.

Auditory hallucinations.

We assessed the occurrence of auditory hallucinations using the following item:

1. **Just before the beep went off** I was hearing voices (that other people cannot hear).

Posttraumatic stress symptoms.

We assessed the occurrence of trauma memory intrusions, avoidance, and hyperarousal using the following items:

Thinking about the traumatic or stressful event(s) we identified as related to your voices…

2. **Since the last beep**, memories of the event(s) came into my head when I did not want them to.

3. **Since the last beep** I have tried hard to avoid thinking about or being reminded of the event (s).

4. **Since the last beep** I have been constantly alert, on edge, irritable, or jumpy.

All EMA items were rated on a scale of 1–7 (1 'not at all' to 7 'a lot'). Our auditory hallucination items have been piloted within a psychosis population (Hartley et al., 2014). The posttraumatic stress symptom items were developed based upon common self-report measures for PTSD and DSM-5 PTSD symptom clusters.

8.6.3 Statistical analysis.

EMA data have a multilevel structure in which multiple observations (level one) are nested within participants (level two). We therefore used hierarchical linear models to account for the non-independence of level one data. Hierarchical linear models for the main EMA analyses were created using HLM 7 (Raudenbusch et al.,

2011). STATA 14 (StataCorp, 2015) was used for any additional participant-level analyses.

Within-person (level one) associations with auditory hallucinations (main effects).

To test our primary hypotheses regarding the within-person relationship between posttraumatic stress symptoms and auditory hallucinations, we transformed our auditory hallucination EMA item into a dichotomous dependent variable, indicating the presence or absence of auditory hallucinations (1=absent, 2-7= present). Analyses were conducted using two-level hierarchical generalised linear models (HGLM) with Bernoulli distribution and logit link function. Two separate models were created; one to estimate the effects of trauma memory intrusions, avoidance, and hyperarousal in the time period immediately preceding the EMA signal (proximal model) and another in the previous time period (lagged model).

Between-person (level 2) moderators of the relationship between posttraumatic stress symptoms and auditory hallucinations (interaction effects).

We initially explored the potential moderating effects of the between-person variables of interest by regressing them onto the residuals of the level one models. Where they had an absolute t-value above two, we entered them as predictors of the level one model coefficients to test our moderation hypotheses.

Model specification.

Full maximum likelihood estimation was used for all models. The effects of time (measurement occasion and time of day) and variables significantly associated with missingness of data (PTSD diagnosis and gender) were explored and controlled for when found to be significant (Black et al., 2012; Bolger & Laurenceau, 2013). The lagged (time-1) dependent variables were also entered into all models to control for

the possibility of serial autocorrelation in the residual errors. Dependent variables and dummy-coded predictors were entered uncentred and continuous predictor variables and covariates were entered person-mean centred at level one (since the main effects of interest were at the within-person level) and grand-mean centred at level two. Slopes were modelled as random effects when indicated by significant level two variance. Robust standard errors were used for all models and improved fit of each model iteration was ensured using the Akaike Information Criterion.

We included all participants in the analysis regardless of how many assessments they had completed, since multilevel models are able to manage unbalanced data. Previous authors have recommended that analysis of EMA data only include participants who have completed at least one-third of assessments (Delespaul, 1995). We therefore conducted a sensitivity analysis excluding participants who completed less than one-third of assessments (n=3) to check this did not alter the significance or magnitude of the results.

Ethical approval for the study was granted by Alfred Health HREC (436/16) and Swinburne University HREC (2016/276). All procedures complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

8.7 Results

8.7.1 Sample

Thirty participants consented to take part in the study. The final sample comprised of 28 participants who completed the EMA schedule (n=1 excluded for current substance dependence, n=1 lost to follow up). Twenty-two (78.6%) of these participants met criteria for a current schizophrenia spectrum disorder and four (14.3%) for a mood disorder with psychotic features. Two participants (7.1%) met

criteria for borderline personality disorder (BPD), with no comorbid axis I diagnosis.
In total seven participants (25%) met criteria for BPD (as either a primary or
comorbid diagnosis). Eleven participants (39.3%) met diagnostic criteria for PTSD.
Seven participants (25%) were rated as having a direct link between their auditory
hallucination content and trauma. Basic demographic and clinical characteristics of
the final sample are shown in Table 6.

Table 6. Participant demographics: Study One (n = 28).

Age, m (SD)	44.96 (9.91)
Gender, n (%)	
Female	18 (64.29)
Male	9 (32.14)
Other	1 (3.57)
Ethnicity, n (%)	
Caucasian	22 (78.57)
Asian	1 (3.57)
Hispanic	2 (7.14)
Aboriginal/ Torres Strait Islander	1 (3.57)
Other	2 (7.14)
Highest level of education, n (%)	
Primary	3 (10.71)
Secondary	7 (25.00)
Diploma	7 (25.00)
Undergraduate	7 (25.00)
Postgraduate	3 (10.71)
Other	1 (3.57)
Index traumatic event type, n (%)	
Childhood sexual abuse	8 (28.57)
Childhood physical abuse	6 (21.43)
Childhood emotional abuse	11 (39.29)
Adulthood sexual abuse	6 (21.43)
Bullying	4 (14.29)
Workplace accident	1 (3.57)
Witnessing death of family member	1 (3.57)
Military trauma	1 (3.57)
PSYRATS AHS, m (SD)	28.21 (6.90)
Number of years heard voices, m (SD)	22.27 (14.32)
Taking anti-psychotic medication, n (%)	
Yes	21 (75.00)
No	5 (17.86)
Missing	2 (7.14)

Legend: m = mean, n = number, PSYRATS-AHS = Psychotic Symptom Rating
Scale – Auditory Hallucinations Subscale, SD = standard deviation.

8.7.2 EMA item descriptives.

EMA data were collected at 1680 time points, with responses completed at 1190 of these (29.17% missing). A two-level HGLM with missingness as a dichotomous dependent variable and time point (0-60) as a predictor showed a significant increase in the likelihood of missing data over the course of the six days (OR = 1.01, $t - 2.73$, $p < 0.006$, 95% CI [1.00, 1.02]).

Auditory hallucinations were reported at 761 (63.95%) time points. Trauma memory intrusions were reported at 623 time points (52.35%), avoidance of trauma reminders at 732 time points (61.51%), and hyperarousal at 757 time points (63.61%). The split-week reliability of EMA items was calculated as the correlation between mean within-person item scores from the first half (days 1-3) and the second half (days 4-6) of the EMA period. Mean levels of the EMA constructs were found to be relatively stable over time.

There is a risk that repeated assessments in EMA studies may alter the frequency or intensity of the variables measured. A series of hierarchical linear regressions with EMA items as the dependent variable and time point as the predictor found no significant associations suggesting that there was no measurement reactivity.

Table 7 and Table 8 provide basic descriptive statistics and within- and between-person correlations between the EMA items.

Table 7. EMA item descriptive statistics.

Item	Mean	Within person SD	Between person SD	% reported (>1)	Split week reliability (r)
AH presence (binary)	0.64	0.31	0.38	64	0.95
Trauma memory intrusions	2.61	1.27	1.48	52.35	0.89
Avoidance	3.39	1.53	1.88	61.51	0.88
Hyperarousal	2.89	1.24	1.60	63.61	0.86

Legend: AH = auditory hallucination, SD = standard deviation

Table 8. Within- and between-person correlations (r) of EMA items.

Item	1	2	3	4
1. AH presence (binary)	1	0.54	0.54	0.62
2. Trauma memory intrusion intensity	0.46	1	0.67	0.46
3. Avoidance	0.37	0.61	1	0.51
4. Hyperarousal	0.52	0.54	0.44	1

Legend: AH = auditory hallucination
Note: Between-person correlations shown as shaded values and within-person correlations shown in white.

8.7.3 Are proximal trauma memory intrusions, avoidance, and hyperarousal associated with auditory hallucinations?

Results from the main effects models are included in Table 9. Proximal (occurring in the hour preceding the EMA signal) trauma memory intrusions were significantly associated with auditory hallucinations. An increase of one point on the trauma memory intrusions scale within the hour prior to the signal increased the likelihood of an auditory hallucination at the signal by 43% on average when proximal avoidance, hyperarousal and auditory hallucinations at the previous time point were controlled. Proximal avoidance and hyperarousal were not significant predictors of auditory hallucinations.

Table 9. Main effects: Study One.

Proximal (within the preceding hour) predictors of AHs[+]	t-statistic	OR	95% CI	*p* value
Trauma memory intrusions	3.40	1.43	1.15, 1.77	0.002
Avoidance	-0.64	0.95	0.81, 1.12	0.529
Hyperarousal	2.01	1.23	0.99, 1.52	0.056
Lagged (60-120 minutes prior) predictors of AHs[+]	t-statistic	OR	95% CI	*p* value
Trauma memory intrusions	1.60	1.10	0.97, 1.26	0.122
Avoidance	0.19	1.01	0.93, 1.10	0.850
Hyperarousal	0.56	1.03	0.94, 1.12	0.573

Legend: AH = auditory hallucination, CI = confidence interval, OR = odds ratio. [+] Holding constant other posttraumatic stress symptoms, and AHs at the previous time point.

8.7.4 Do lagged trauma memory intrusions, avoidance, and hyperarousal predict auditory hallucinations?

Lagged (occurring in the previous time period) trauma memory intrusions, avoidance, and hyperarousal were not significant predictors of auditory hallucinations.

8.7.5 Moderators of the relationship between trauma memory intrusions, avoidance, hyperarousal, and auditory hallucinations.

The nature of the link between auditory hallucination content and the index traumatic event was a significant moderator of the relationship between both proximal and lagged trauma memory intrusions and auditory hallucinations (proximal ß = 0.50, t-ratio = 2.71, $p = 0.01$, lagged ß = 0.28, t-ratio = 3.07, $p < 0.01$). Those with a direct link between the content of their auditory hallucinations and the index traumatic event showed on average a 101% increase in the odds of having an auditory hallucination

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with every one point increase in proximal trauma memory intrusions, as opposed to 23% for those without this direct link, and on average a 37% increase in the odds of having an auditory hallucination with every one-point increase in lagged trauma memory intrusions, as opposed to 3% for those without this direct link, when proximal avoidance, hyperarousal, and auditory hallucinations at the previous time point were controlled. Figure 2 shows the relationship between trauma memory intrusions and auditory hallucinations for those with and without a direct link between the content of their auditory hallucinations and the index traumatic event.

In addition, having a PTSD diagnosis significantly moderated the relationship between avoidance and auditory hallucinations (ß = 0.14, t-ratio = 2.28, p =0.03)**.** Those with PTSD showed a 7% increase in the odds of having an auditory hallucination with each one-point increase in lagged avoidance on average as opposed to a 7% decrease for those without PTSD when proximal avoidance, hyperarousal, and auditory hallucinations at the previous time point were controlled. Figure 3 shows the relationship between avoidance and auditory hallucinations for those with and without a PTSD diagnosis.

The disorganisation and intrusiveness of the trauma memory was not a significant moderator of the relationship between momentary posttraumatic stress symptoms and auditory hallucinations.

Figure 2. The link between auditory hallucination content and the index trauma memory as a moderator of the relationship between lagged trauma memory intrusions and auditory hallucinations.
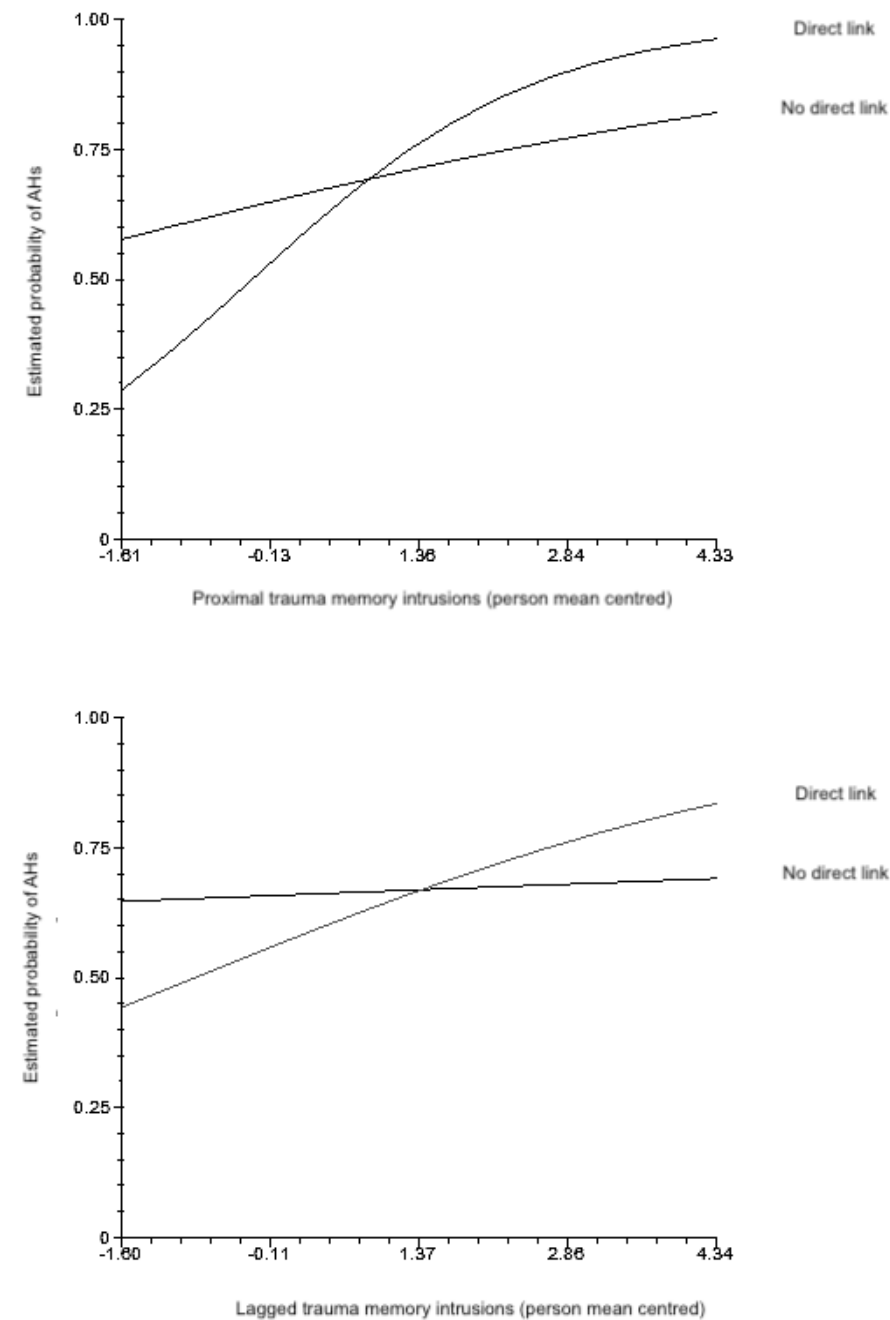
Note: posttraumatic avoidance and hyper arousal set to equal the mean value for each person.

Figure 3. PTSD diagnosis as a moderator of the relationship between lagged avoidance and auditory hallucinations.
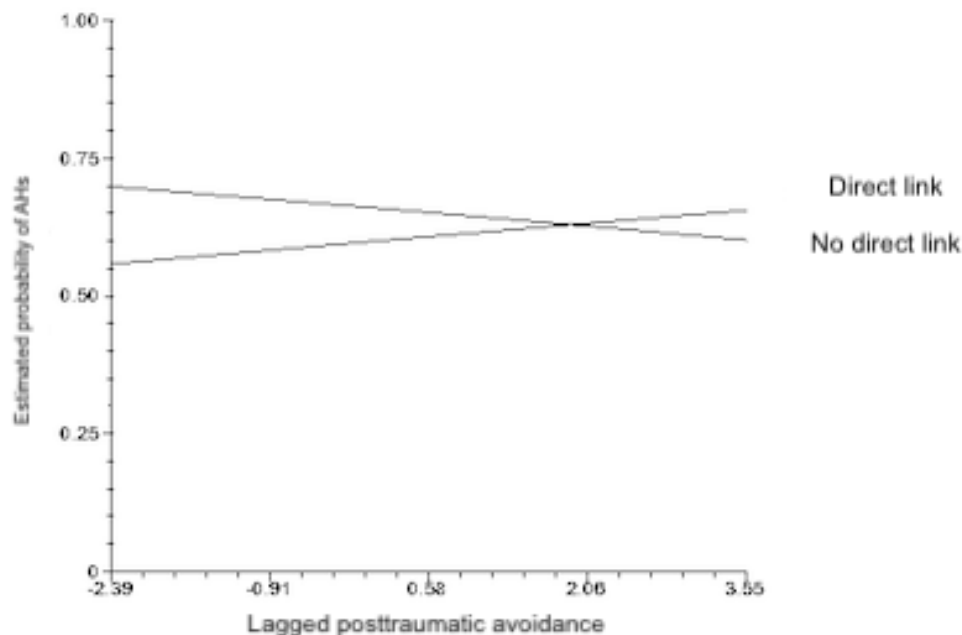
Note: trauma memory intrusions and hyper arousal set to equal the mean value for each person

8.7.6 Sensitivity analysis

The sensitivity analyses conducted only on the sample who completed over 33% of the EMA assessment points (*n*=25) obtained the same pattern of results.

8.8 Discussion

As hypothesised, we found that proximal trauma memory intrusions were associated with auditory hallucinations. Increased severity of trauma memory intrusions within the previous hour significantly increased the likelihood of an auditory hallucination. This relationship was particularly marked for people with a direct link between the content of their auditory hallucinations and the content of the index traumatic event. Trauma memory intrusions that were more distal (occurring 60 to 120 minutes prior) were not a significant predictor of auditory hallucinations overall, however those with a direct link between the content of the traumatic event and their auditory hallucinations did show a significant relationship. This supports

previous cross-sectional research that has found a relationship between aggregate

trauma memory intrusions and auditory hallucinations (Peach et al., 2018), and

extends these findings to show moment-to-moment associations between trauma

memory intrusions and auditory hallucinations. This momentary association provides

support for the theory that trauma-related auditory hallucinations are shaped by

trauma memory intrusions arising from episodic memories that have been poorly

contextualized and elaborated in autobiographical memory. Consistent with this, the

association was strongest for the subgroup who had a direct link between the content

of their trauma memory and their auditory hallucinations. For these people, trauma

memory intrusions significantly increase the likelihood of auditory hallucinations and

this effect endures over a longer period of time.

   Contrary to our hypotheses and theoretical models of trauma-related auditory

hallucinations (Hardy, 2017; Morrison, 2003), posttraumatic avoidance did not predict

auditory hallucinations overall, however those meeting criteria for PTSD did have

significantly greater likelihood of auditory hallucinations following increased

avoidance in the previous 60 to 120 minutes. This provides partial support for

previous research suggesting that posttraumatic avoidance is associated with auditory

hallucinations (Hardy et al., 2016; Powers et al., 2016), however our findings suggest

that the association between avoidance and auditory hallucinations in the flow of daily

life occurs distally (i.e. only in the lagged analysis) and only in those meeting criteria

for PTSD. Avoidance maintains trauma memory intrusions in PTSD (Ehlers & Steil,

1995) and Morrison's (2003) theory of trauma and psychosis also implicates

avoidance as a maintaining factor for trauma memory intrusions and thus also

auditory hallucinations. Therefore one (speculative) explanation for this more distal

effect of avoidance only in the PTSD group is that avoidance of particularly intrusive

memories (characteristic of those with PTSD) has a delayed 'rebound' effect in which avoidance increases the likelihood of intrusive trauma memories (and therefore auditory hallucinations). One important difference between our methods and those of previous studies is that we based our measurement of avoidance on DSM-5 PTSD criteria, whereas previous studies used DSM-IV. Our measure of avoidance therefore did not capture numbing/ dissociative responses (since they are no longer included in the avoidance symptom cluster in DSM-5), which may have driven previous relationships found between avoidance and auditory hallucinations (Hardy et al., 2016; Powers et al., 2016).

Our finding that hyperarousal did not predict the occurrence of auditory hallucinations was counter to our hypotheses and does not support theories of trauma-related auditory hallucinations (Dodgson & Gordon, 2009; Hardy, 2017), however it should be noted that we assessed hyperarousal as a single construct (based on a composite of the DSM-5 hyperarousal symptom cluster). It is possible that we did not find an association because we included hyperarousal constructs in addition to hypervigilance constructs and that these are less directly relevant to auditory hallucinations.

8.8.1 Limitations

When interpreting the results of this study, some potential methodological limitations should be considered. Firstly, although the 'micro-longitudinal' approach used in this study builds on cross-sectional research by explicating moment-to-moment associations between posttraumatic stress symptoms and auditory hallucinations in daily life, the relationships described are still only at the level of association. Given that main effects were only significant for trauma memory intrusions in the proximal analysis and not in the lagged analysis it is not possible to

determine the temporal ordering of these experiences. It is also possible that there are other confounding variables (such as negative affect, activated negative self/ other beliefs, paranoia, anxiety or rumination) that explain the associations between trauma memory intrusions and auditory hallucinations.

Additionally, our EMA items assessing posttraumatic stress symptoms were created specifically for this study and have not been previously validated. Notably, we used single EMA items to assess quite complex phenomena that may have better been assessed using composite measures.

Recruitment for this study took place in parallel with another adjoining therapy trial. The inclusion criteria for this therapy trial meant that participants had to have made some conceptual links between their traumatic event and their auditory hallucinations. Thus, the sample in this study consisted of people who themselves believed that there was a link between their trauma and their auditory hallucinations. The findings here may therefore not be generalisable to all people with auditory hallucinations with a background of traumatic events but may be specific to those who have made connections between their traumatic events and auditory hallucinations.

8.8.2 Clinical implications

Our finding that trauma memory intrusions are associated with the occurrence of auditory hallucinations suggests that psychological therapies that ameliorate trauma memory intrusions may be helpful for distressing trauma-related auditory hallucinations. To date there have not been any trials of evidence-based trauma-focused therapies for PTSD with auditory hallucinations as a primary treatment target, however indications from trials using these therapies to treat PTSD in people with psychosis suggest only small (secondary) effects on auditory hallucinations (Brand,

McEnery, Rossell, Bendall, & Thomas, 2017). The findings here suggest that trauma focused therapies will have most utility for a small group of people with a direct link between the content of the trauma and the content of their auditory hallucinations, since the relationship between trauma memory intrusions and auditory hallucinations appears most potent in this group.

8.8.3 Future research

Future research can build on our finding that trauma memory intrusions have an association with auditory hallucinations in the flow of daily life by controlling for other potentially confounding variables such as negative affect, activated negative self/ other beliefs, rumination, and paranoia. It will also be important to further assess the putative role of posttraumatic avoidance and hyperarousal outlined in theoretical models of trauma-related auditory hallucinations using more precise assessments of hypervigilance and of numbing/ dissociative aspects of posttraumatic avoidance.

Chapter Nine: Do Trauma-Focused Psychological Interventions Have an Effect

on Psychotic Symptoms? A Systematic Review and Meta-analysis (Peer

Reviewed Publication Three).

9.1 Preamble to Publication Three

Publication Three outlines the rationale, methods, and findings of Study Two,

a systematic review and meta-analysis examining whether trauma-focused

interventions used to treat PTSD in psychosis populations have secondary effects on

psychotic symptoms. This study aimed to use pre-existing data from studies using

trauma-focused therapies in psychosis populations to provide initial indications of the

causal role of PTSD symptoms in psychotic experiences, and the potential for trauma-

focused interventions as treatments for trauma-related psychotic symptoms.

Publication Three has been published in the journal *Schizophrenia Research*,

which is a highly ranked international journal. The 2018 impact factor for

Schizophrenia Research was 4.569. A copy of the article in its published form is

provided in Appendix V. The 'Author Indication Form', which details the nature and

extent of the candidate and co-authors' contributions to this manuscript is included in

Appendix VI. The results of this study were also presented as an open paper at the

World Psychiatric Association Thematic Congress, Melbourne, 2019. The complete

citations are as follows:

Brand, R.M., McEnery, C., Bendall, S., Rossell, S.L. & Thomas, N. (2018) Do

trauma-focused psychological interventions have an effect on psychotic symptoms? A

systematic review and meta-analysis. *Schizophrenia Research*, 195:13-22.

doi:10.1016/j.schres.2017.08.037.

Brand, R.M., McEnery, C., Bendall, S., Rossell, S. & Thomas, N. (2018). Do trauma-focused psychological interventions have an effect on psychotic symptoms? A systematic review and meta-analysis, World Psychiatric Association Thematic Congress, Melbourne, Australia.

9.2 Abstract

There is growing recognition of the relationship between trauma, posttraumatic stress disorder (PTSD) and psychosis. There may be overlaps in causal mechanisms involved in the development of PTSD and psychosis following traumatic or adverse events. Trauma-focused treatments found to be effective in treating PTSD may therefore represent a new direction in the psychological treatment of psychosis. This systematic review examined the literature on trauma-focused treatments conducted with people with schizophrenia spectrum or psychotic disorders to determine effects on psychotic symptoms. Secondary outcomes were symptoms of PTSD, depression, and anxiety. Twenty-five studies were included in the review, with 12 being included in the meta-analysis. Trauma-focused treatments had a small, significant effect ($g = 0.31$, CI [0.55, 0.06]) on positive symptoms immediately post treatment, but the significance and magnitude of this effect was not maintained at follow up ($g = 0.18$, CI [0.42, -0.06]). Trauma-focused treatments also had a small effect on delusions at both post treatment ($g = 0.37$, CI [0.87, -0.12]) and follow up ($g = 0.38$, CI [0.67, 0.10]), but this only reached significance at follow up. Effects on hallucinations and negative symptoms were small and nonsignificant. Effects on PTSD symptoms were also small (post treatment $g = 0.21$, CI [0.70, -0.27], follow up $g = 0.31$, CI [0.62, 0.00]) and only met significance at follow up. No significant effects were found on symptoms of depression and anxiety. Results show promising

effects of trauma-focused treatments for the positive symptoms of psychosis, however further studies developing and evaluating trauma-focused treatments for trauma-related psychotic symptoms are needed.

9.3 Key Words

Psychosis; Schizophrenia; Posttraumatic Stress Disorder; Trauma; Treatment; Meta-analysis.

9.4. Introduction

There is mounting evidence that exposure to traumatic or adverse experiences in childhood represents a significant risk factor in the development of psychosis (Bendall et al., 2008; Read et al., 2001; Varese et al., 2012) and there is thematic correspondence between the content of psychotic experiences and significant past life events (Corstens & Longden, 2013; Hardy et al., 2005; McCarthy-Jones et al., 2014). There is also compelling evidence to suggest a relationship between posttraumatic stress disorder (PTSD, arguably the 'hallmark' disorder caused by traumatic events) and psychosis, including high rates of comorbidity (Sareen et al., 2005) and PTSD being a risk factor for the development of psychosis (Okkels et al., 2017).

This relationship suggests similar mechanisms could be involved in psychotic experiences and symptoms of PTSD (Morrison et al., 2003). For example, it has been proposed that auditory hallucinations are a type of posttraumatic intrusion, contributed to by contextual processing difficulties (Hardy, 2017; Steel et al., 2005). Additionally, dissociation (Moskowitz & Corstens, 2007) and negative posttraumatic beliefs (Gracie et al., 2007) have been implicated in the development of auditory hallucinations. Similar psychological mechanisms are also implicated in the development of delusional experiences and PTSD symptoms following a traumatic

event (Freeman et al., 2013), whilst negative symptoms have been conceptualised as manifestations of trauma-related avoidance (McGorry, 1991).

Trauma-focused interventions are effective in treating PTSD (Bisson et al., 2007). Given potential mechanistic overlaps between PTSD and psychosis, trauma-focused treatments represent a new direction in treatment development for psychosis. This aligns with mental health service-user calls for therapeutic approaches that consider psychosis in the context of past life experiences (Corstens et al., 2014). Recently, researchers have begun to apply trauma-focused treatments to comorbid PTSD and other trauma-related symptoms in people with psychotic disorders. While evidence remains too limited for a Cochrane review to draw any meaningful conclusions (Sin, Spain, Furuta, Murrells, & Norman, 2017), two recent reviews have concluded that trauma-focused treatments can be used safely and effectively reduce PTSD symptoms in this population (Sin & Spain, 2016; Swan, Keen, Reynolds, & Onwumere, 2017). Emerging data also suggests that trauma-focused treatments may have an impact on psychotic symptoms, but this is yet to be systematically synthesized across studies. We examined the literature on trauma-focused treatments conducted within psychosis populations to determine whether these interventions have an effect on psychotic symptoms.

9.5 Methods

The review was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO), protocol no: CRD42016035827 and is reported in accordance with PRISMA guidelines.

9.5.1 Eligibility criteria

Table 10 outlines the eligibility criteria used.

Table 10. Inclusion and exclusion criteria: Study Two

Inclusion criteria	Exclusion criteria
Studies of participants with psychosis (defined by a psychiatric diagnosis of a schizophrenia spectrum disorder or psychotic disorder OR scores above clinical cut off for hallucinations, delusions or negative symptoms on validated clinical interviews or measures)	Studies with nonclinical samples
Controlled or uncontrolled treatment studies with quantitative outcome data derived from psychometrically validated measures.	Studies without quantitative outcome data or from which quantitative data are derived from scales which are not psychometrically validated
Studies testing trauma-focused treatments with an evidence base for PTSD as outlined in the Australian Guidelines for the treatment of PTSD (Phoenix Australia, 2013, and defined in this review as any psychological therapy that predominantly uses trauma-focused cognitive-behavioural techniques and including EMDR, PE, trauma focused cognitive therapy, trauma focused CBT, and cognitive processing therapy)*	Studies using non trauma-focused treatments (i.e. those which do not discuss the content or themes of the index traumatic event(s) during the treatment)

* Note: we chose to include any study using trauma-focused treatments to treat posttraumatic symptoms in people with psychosis, irrespective of PTSD diagnosis or index trauma.

9.5.2 Information sources

Literature searches were conducted using five databases: PsycINFO, PubMed, EMBASE, CINAHL, and The Cochrane Library. In addition, the WHO international clinical trials registry platform and references of included articles were searched.

9.5.3 Search terms

The search strategy involved: 1) terms relating to schizophrenia spectrum or psychotic disorders, and 2) terms relating to trauma-focused psychological interventions. Literature was searched from the inception of the databases until 25th March 2016. Articles were required to be in English.

9.5.4 Study Selection

Record titles and abstracts were screened for inclusion by one author. Full text records were assessed for inclusion independently by two authors, with 83% agreement. Discrepancies were resolved in discussion with a third author.

9.5.5 Data collection process and data items

The following data were extracted from each study: 1) study design, 2) intervention and comparison 3) participant characteristics, 4) treatment format 5) therapist characteristics, 6) primary outcomes, 7) secondary outcomes, 8) treatment retention, and, 9) main results.

9.5.6 Risk of bias in individual studies

Risk of bias was assessed independently by two authors (83% initial agreement) using The Cochrane Collaboration tool (Higgins et al., 2011a), rating each study as 'low', 'high', or 'unclear' risk for the following criteria; 1) random sequence generation, 2) allocation sequence concealment, 3) masking, 4) incomplete outcome data, and 5) selective reporting. Uncontrolled studies automatically received a 'high risk' rating on criteria one to three.

9.5.7 Synthesis of results

Uncontrolled and controlled studies were subject to meta-analytic synthesis using Comprehensive Meta-analysis 3.0. Primary outcomes were the severity of positive and negative symptoms of psychosis, and specifically hallucinations and delusions[2]. Secondary outcomes were PTSD, depression and anxiety symptom severity. A decision to use random effect models was made a-priori, given the anticipated heterogeneity of study interventions and designs. Hedges g was used to calculate effect sizes. Analyses were conducted to calculate both pre-post treatment effects (across all studies), and between-groups treatment effects (in randomised controlled trials only). Pre-post treatment effect sizes were calculated using change scores, with standard deviations of change scores as the denominator. Since repeated measures correlations were not available, a correlation of 0.70 was assumed, as suggested by Rosenthal (1993). Between-group effect sizes were calculated using posttest means and pooled standard deviations. Where means and standard deviations were not available, effect sizes were calculated using other data. Heterogeneity of results was analysed using the I^2 statistic.

Three studies had a 'severe mental illness' sample, including participants without psychosis (Mueser et al., 2007; Mueser et al., 2015; Mueser et al., 2008). The authors of these studies either provided disaggregated means and standard deviations for the psychosis subgroup or access to their raw data. Linear mixed models provided intent-to-treat estimated marginal means from this raw data. Analyses were conducted for two time points, post treatment and follow up (including any follow ups conducted

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[2] Our original intention was to measure hallucinations, delusions and negative symptoms as primary outcomes, as outlined in the PROSPERO protocol. On collation of the results it became clear that the measurement of hallucinations and delusions was more commonly reflected in an aggregate measure of positive symptoms. A decision was therefore made to include positive symptoms as a primary outcome.

between one and six months following treatment). For studies that included more than one follow up in this timeframe, the time-points were pooled using the method described by Borenstein (2009). Positive symptom scores were taken from positive scale scores of the Positive and Negative Syndrome Scales or Brief Psychiatric Rating Scales, or, when only separate measures of hallucinations and delusions were available, by pooling available positive symptom scores into a single variable, also using the Borenstein (2009) method.

9.5.8 Quality assessment across studies

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used by two raters to collaboratively assess the quality of evidence for each outcome and give an overview of confidence in the effect size (Guyatt et al., 2008). Ratings fall into four categories (high, moderate, low and very low) based on: risk of bias, consistency, directness, precision, and publication bias.

9.6 Results

The database search yielded 4399 records. Once duplicates were removed, 3236 records were screened on titles and abstracts. Forty one full text records were assessed. An additional two 'in press' studies were identified through contact with the authors (de Bont et al., 2016; Steel et al., 2017). Twenty-five articles were included in the final review. Figure 4 displays the PRISMA flow-chart of the selection process.

Figure 4. PRISMA flow-chart of the selection process in Study Two.
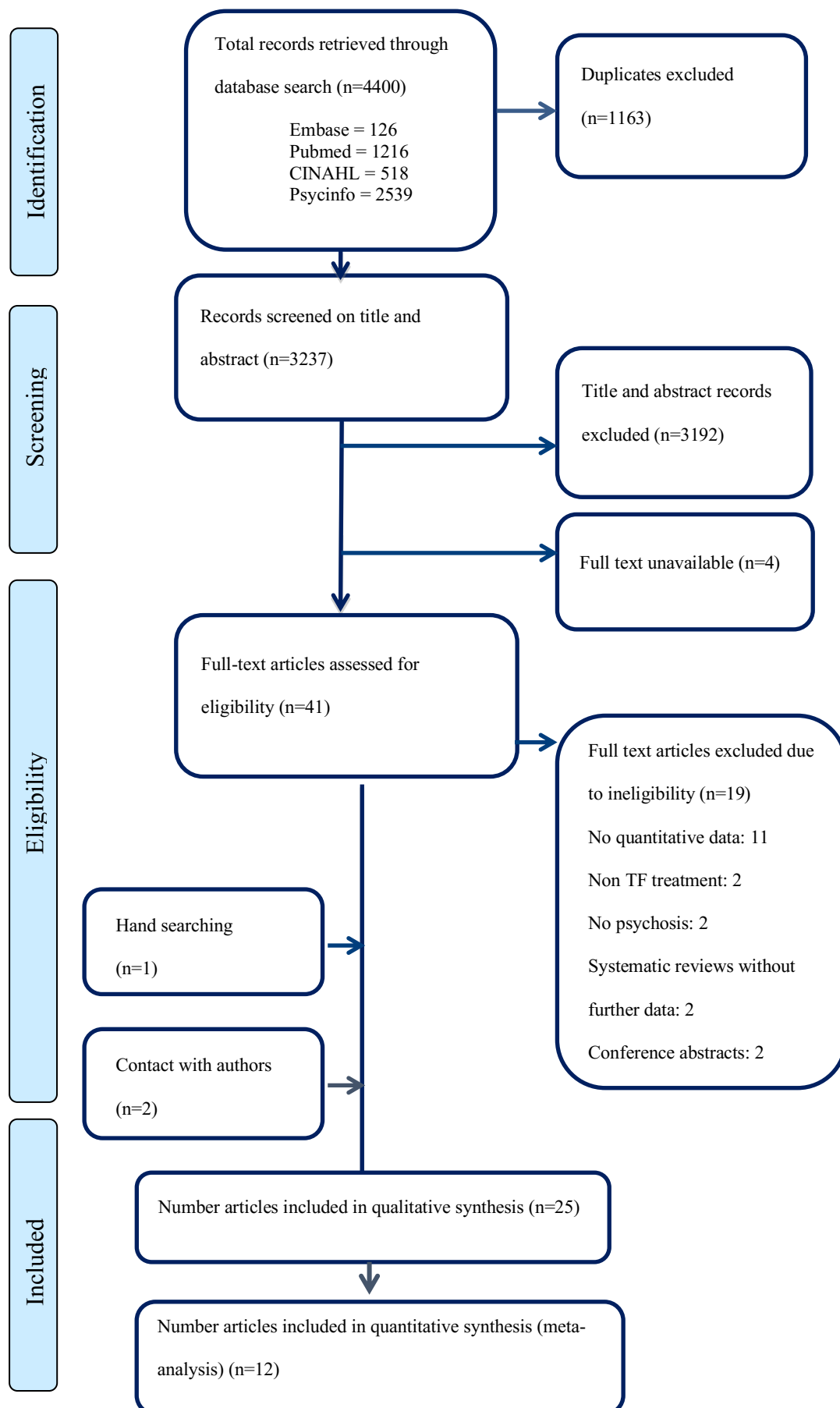
9.6.1 Study characteristics

Table 11 provides an overview of the 25 original articles included in the review. Case studies ($n = 8$) are not included in the synthesis of results but are presented in Table 11 for readers' interest. Three articles related to the same primary study (de Bont et al., 2016; van den Berg et al., 2015a, 2015b), meaning that in total, 15 controlled and uncontrolled studies were included. Three studies were excluded from the meta-analysis due to insufficient data or small sample size (Lu, 2009; Rosenberg, Mueser, Jankowski, Salyers, & Acker, 2004; Trappler & Newville, 2007). The meta-analytic synthesis therefore included 12 controlled and uncontrolled studies with a total of 520 participants. Follow up ranged in length from one to 12 months; however only one study (Mueser et al., 2015) included a 12 month follow up, with the remainder having six months as their longest follow up point. This 12 month follow up was therefore not included in the meta-analysis. All controlled studies used a treatment as usual (TAU) control group, other than one which used a written exercise regarding non emotional topics (Bernard, 2006) and one which used a brief, three session psycho-education and breathing retraining comparison (Mueser et al., 2015). One study (Kim et al., 2010) used two control groups, one TAU group and one using a progressive muscle relaxation intervention. For this study, only the TAU control was used in the meta-analysis.

Table 11. Study characteristics: Study Two.

Study	Design	n	Diagnoses	Mean age (SD)	% Male	Trauma focused treatment delivered+	Planned number of sessions (Mean delivered)	Comparison condition	% attrition at longest follow up	Relevant outcome measures	Follow up period (months) from end of treatment	Risk of bias assessment	Risk of bias
Case Studies													
Arens, 2015	CS	1	PTSD with comorbid hallucinations	45 (0)	100	TMT	N/A (29)	N/A	0	CAPS PCL-M Daily diaries of hallucinations	3		High
Calcott et al., 2004	CS	2	Psychosis with comorbid PTSD	39.5 (5.5)	0	TF-CT/ Imagery rescripting	N/A (14.5)	N/A	0	IES BDI-II CPRS SANS	0		High
Hamblen et al., 2004	CS	3	Bipolar disorder or Schizoaffective disorder, with comorbid PTSD	46 (7.3)	66	CR	N/A (14.7)	N/A	0	BPRS CAPS	3		High
Hardy et al., 2013	CS	1	Schizoaffective disorder with comorbid PTSD	54 (0)	0	CR	N/A (16)	N/A	0	CAPS BDI-II	6		High
Kevan et al., 2007	CS	1	Schizophrenia with comorbid PTSD	31 (0)	0	Written trauma elaboration and CR	N/A (7)	N/A	0	PDS BDI-II	1		High
Marcello et al., 2009	CS	1	Schizoaffective Disorder	55 (0)	100	CR	N/A (16)	N/A	0	PCL-S BDI-II	0		High
Mauritz et al., 2009	CS	1	Complex-PTSD with psychotic disorder	47 (0)	0	Stabilisation and PE	N/A (40)	N/A	0	DTS	0		High
Smith & Steel, 2009	CS	1	Schizophrenia	23 (0)	100	TF-CBT	N/A (16)	N/A	0	PSYRATS SAPS	None		High

Study	Design	N	Population	Age M (SD)	%	Intervention	Sessions	Comparison		Measures	Follow-up	Risk of bias					Overall
1. Bernard et al., 2006	RCT	23	First episode psychosis	24.7 (6.2)	60.9	Written emotional disclosure	3 (3)	Written essay on non-emotional topics	4	IES-R HADS	1-1.5	L	L	L	L	L	Low
2. de Bont et al, 2013	MBS	10	Schizophrenia, Schizoaffective disorder or psychosis NOS, with comorbid PTSD	43.6 (10.8)	20	PE or EMDR	12 (10.3)	Participants' baseline score served as their own comparison	20	PSYRATS CAPS	3	U	U	U	L	L	Unclear
3. Frueh et al., 2009	PP	20	Schizophrenia or Schizoaffective disorder, with comorbid PTSD	42.3 (8.4)	25	Multi-component CBT including exposure therapy	22 (17.1)	N/A	35	CAPS HAM-D HAM-A	3	H	H	H	H	L	High
4. Grubaugh et al., 2016	PP	34	Psychotic disorder, Bipolar disorder or Mood disorder with psychotic features, with comorbid PTSD	47.8 (13.4)	88.2	PE	10 (7.2)	N/A	NR	CAPS PCL	6	H	H	H	H	L	High
5. Jackson et al., 2009	RCT	66	First episode psychosis	23.3 (4.6)	74.2	CRI	< 26 (11)	TAU	30.3	IES CDS	6	L	L	L	H	H	High
6. Kim et al, 2010	RCT	45	Schizophrenia (inpatients)	32.6 (6.7)	27	EMDR	3 (3)	PMR or TAU	35.6	PANSS HAM-D HAM-A	3	U	U	L	L	L	Unclear
7. Lu et al., 2009	PP	3*	Schizophrenia or Schizoaffective disorder with comorbid PTSD	42.5 (8.8)	42	CR	12-16 (14.4)	N/A	14.3	BPRS PCL BDI-II	3, 6	H	H	H	H	L	High

8. Mueser et al., 2007	PP	10*	Schizophrenia or Schizoaffective disorder with comorbid PTSD	42.9 (7.93)	21	Group CR	21 (16)	N/A	48.8	PCL BDI-II	3	H H L L L High
9. Mueser et al., 2008	RCT	17*	Schizophrenia or Schizoaffective disorder with comorbid PTSD	44.2 (10.6)	21.3	CR	12-16 (NR)	TAU	50.9	BPRS CAPS BDI-II BAI	3, 6	L L L L L Low
10. Mueser et al., 2015	RCT	67*	Schizophrenia or Schizoaffective disorder with comorbid PTSD	43.0 (10.5)	31.3	CR	12-16 (NR)	Breathing retraining and psycho education (3 sessions)	22.4	PANSS CAPS-S$ BDI-II BAI	6, 12	L L L L L Low
11. Rosenberg et al., 2004	PP	10*	Schizophrenia, Schizoaffective disorder or psychotic disorder NOS with comorbid PTSD	48 (8.13)	46	CR	12-16 (NR)	N/A	36.8	BPRS CAPS	3	H H H H L High
12. Steel et al., 2016	RCT	61	Schizophrenia, schizoaffective disorder with comorbid PTSD	42.3 (10.2)	62.3	CR	(12.3)	TAU	23	PANSS PSYRATS CAPS-S BDI BAI	6	L L L L L Low
13. Trappler et al., 2007	NRCT	24	Schizophrenia or Schizoaffective disorder with comorbid PTSD	NR	NR	Group STAIR	12 (NR)	Group SP	NR	BPRS IES	None	H H U H U High
14. van den Berg et al., 2012	PP	27	Schizophrenia spectrum or psychotic disorders with comorbid PTSD	45 (9.4)	55.5	EMDR	6 (4.72)	N/A	18.5	PSYRATS GPTS CAPS BDI-II	None	H H H L L High

										BAI		
15. van den Berg et al. 2015a (includes van den Berg et al., 2015b & de Bont et al., 2016)	RCT	155	Schizophrenia spectrum or psychotic disorders with comorbid PTSD	41.2 (10.5)	45.8	EMDR or PE	8 (7.5)	WL +TAU	17.4	CAPS BDI PSYRATS GPTS	6	L L L L L Low

Note: CS = Case study, RCT = Randomised Controlled Trial, MBS = Multiple Baseline Study, PP = pre-post study (single group), NRCT = Non-randomised Controlled Trial, TMT = Trauma Management Therapy, NR = not reported, PTSD = Posttraumatic Stress Disorder, CAPS = Clinician Administered PTSD Scale, PCL-M = PTSD checklist – Military version, HADS = Hospital Anxiety and Depression Scale, TF-CT = Trauma Focused Cognitive Therapy, IES = Impact of Events Scale, BDI-II = Beck Depression Inventory-II, CR = Cognitive Restructuring, BPRS = Brief Psychiatric Rating Scale, CRI = Cognitive Recovery Intervention, PMR = Progressive Muscle Relaxation, TAU = treatment as usual alone, DTS = Davidson Trauma Scale, BAI = Beck Anxiety Inventory, PANSS = Positive and Negative Syndrome Scale, CDS = Calgary Depression Scale, CAPS-S = CAPS – Schizophrenia version, TF-CBT = Trauma Focused Cognitive Behavioural Therapy, PSYRATS = Psychotic Symptom Rating Scale, SAPS = Scale for the Assessment of Positive Symptoms, SANS = Scale for the Assessment of Negative Symptoms, WL = Waitlist, STAIR = Skills Training in Affect and Interpersonal Regulation, GPTS = Green Paranoid Thoughts Scale, SP = Supportive Pychotherapy, N/A = not applicable

+All treatments were delivered in addition to treatment as usual

* This N includes only those with psychosis. The full sample of this study included a larger N encompassing participants with 'severe mental illness'. The figures for mean age, sex, mean number of sessions and attrition rates relate to the full sample, since disaggregated data for these study details were not available.

$ Only categorical data on this measure were available from the original authors, therefore this study could not be included in the analyses of PTSD symptom severity.

9.6.2 Risk of bias within studies

Table 11 shows the risk of bias assessments for each study. There was significant variability in the risk of bias of the studies, with only five studies being considered at low risk of bias.

9.6.3 Synthesis of results

Table 12 displays the effect sizes from each analysis. Further, forest plots for between-group analyses of primary outcomes are shown in Figure 5.

Primary outcomes

Pre-post analyses indicated significant post treatment effects on positive symptoms (small effect) and delusions (small effect), but not hallucinations (small effect) or negative symptoms (small effect). At follow up, effects for positive symptoms (medium effect), delusions (medium effect) and hallucinations (small effect) were significant, but those for negative symptoms remained nonsignificant (small effect).

In the between-groups analyses, we first considered effects on positive symptoms. A small, significant effect was seen at post treatment, but this was not maintained at follow up. In considering delusions and hallucinations separately, small effects for delusions were found at both post treatment and follow up, but these only reached significance at follow up, whereas effects for hallucinations were negligible and nonsignificant at both time points. Effects for negative symptoms were small and did not reach significance.

Table 12. Summary of findings: Study Two.

Outcome	Time point	n	Studies*	g	95% CI	p	I^2	GRADE rating
Uncontrolled, pre-post								
Positive symptoms	Post treatment	7	2,6,9,10,12, 14,15	0.44	[0.66, 0.24]	<0.001	63.25	Very low confidence
	Follow up	6	2,6,9,10,12,15	0.53	[0.83, 0.23]	0.001	79.53	Very low confidence
Negative Symptoms	Post treatment	4	6,9,10,12	0.28	[0.79, -0.23]	0.283	88.39	Very low confidence
	Follow up	4	6,9,10,12	0.44	[1.08, -0.20]	0.177	91.94	Very low confidence
Delusions	Post treatment	4	2,12,14,15	0.36	[0.61, 0.11]	0.005	51.69	Very low confidence
	Follow up	3	2,12,15	0.53	[0.66, 0.40]	<0.001	00.00	Low confidence
Hallucinations	Post treatment	4	2,12,14,15	0.23	[0.47, -0.01]	0.059	45.19	Very low to low confidence
	Follow up	3	2,12,15	0.24	[0.41, 0.08]	0.003	00.00	Low confidence
PTSD	Post treatment	9	2,3,4,5,8,9,12,14,15	0.62	[0.94, 0.29]	<0.001	87.72	Very low confidence
	Follow up	9	1,2,3,4,5,8,9,12,15	0.68	[1.01, 0.35]	0.002	94.47	Very low confidence
Depression	Post treatment	9	3,5,6,8,9,10,12,14,15	0.46	[0.64, 0.28]	<0.001	65.19	Very low confidence
	Follow up	9	3,5,6,8,9,10,12,14,15	0.50	[0.74, 0.25]	<0.001	78.76	Very low confidence
Anxiety	Post treatment	6	3,6,9,10,12,14	0.36	[0.50, 0.22]	<0.001	00.00	Low confidence
	Follow up	6	1,3,6,9,10,12	0.48	[0.61, 0.28]	<0.001	19.49	Low confidence

Controlled, between-group								
Positive Symptoms	Post treatment	5	6,9,10,12,15	0.31	[0.55, 0.06]	0.014	00.00	High confidence
	Follow up	5	6,9,10,12,15	0.18	[0.42, -0.06]	0.148	00.00	High confidence
Negative Symptoms	Post treatment	4	6,9,10,12	-0.08	[-0.46, 0.61]	0.774	66.25	Very low confidence
	Follow up	4	6,9,10,12	0.12	[0.43, 0.18]	0.434	05.74	Moderate confidence
Delusions	Post treatment	2	12,15	0.37	[0.87, -0.12]	0.139	62.98	Moderate confidence
	Follow up	2	12,15	0.38	[0.67, 0.10]	0.008	00.00	High confidence
Hallucinations	Post treatment	2	12,15	0.14	[0.82, -0.54]	0.692	72.77	Low confidence
	Follow up	2	12,15	-0.06	[0.29, -0.42]	0.724	00.00	Moderate confidence
PTSD	Post treatment	4	5,9,12,15	0.21	[0.70, -0.27]	0.388	71.72	Moderate confidence
	Follow up	5	1,5,9,12,15	0.31	[0.62, 0.00]	0.049	36.68	High confidence
Depression	Post treatment	6	5,6,9,10,12,15	0.10	[0.47, -0.27]	0.589	65.53	Low to moderate confidence
	Follow up	7	1,5,6,9,10,12,15	0.06	[0.33, -0.21]	0.659	40.43	Low to moderate confidence
Anxiety	Post treatment	4	6,9,10,12	0.05	[0.24, -0.34]	0.741	00.00	Moderate confidence
	Follow up	5	1,6,9,10,12	0.01	[0.28, -0.27]	0.950	00.00	Moderate confidence

Note: Controlled, between-group and uncontrolled, pre-post effect sizes are standardized using different standard deviation denominators. This means that they are not directly comparable. * Study codes are given in Table11.

Figure 5. Forest plots for between-group controlled analyses of primary outcomes

Between group analysis for positive symptoms at post-treatment

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
						Statistics for each study				
Treatment vs control	Kim et al. 2010	Positive	Post treatment	0.675	0.366	0.134	-0.042	1.392	1.846	0.065
Treatment vs control	Mueser et al. 2008	Positive	Post treatment	0.286	0.470	0.221	-0.635	1.208	0.609	0.543
Treatment vs control	Mueser et al. 2015	Positive	Post treatment	0.089	0.242	0.059	-0.385	0.563	0.368	0.713
Treatment vs control	van den Berg et al. 2015	Combined	Post treatment	0.543	0.224	0.050	0.104	0.982	2.422	0.015
Treatment vs control	Steel et al. 2016	Combined	Post treatment	0.067	0.254	0.064	-0.430	0.564	0.264	0.792
				0.305	0.124	0.015	0.061	0.549	2.453	0.014

Hedges's g and 95% CI

-1.50   -0.75   0.00   0.75   1.50

Favours Control   Favours Treatment

Between group analysis for positive symptoms at follow-up

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
						Statistics for each study				
Treatment vs control	Kim et al. 2010	Positive	Follow-up	0.463	0.360	0.130	-0.243	1.170	1.286	0.198
Treatment vs control	Mueser et al. 2008	Positive	Combined	0.184	0.469	0.220	-0.735	1.103	0.393	0.694
Treatment vs control	Mueser et al. 2015	Positive	Follow-up	0.100	0.242	0.059	-0.374	0.574	0.414	0.679
Treatment vs control	van den Berg et al. 2015	Combined	Follow-up	0.136	0.222	0.049	-0.299	0.570	0.612	0.540
Treatment vs control	Steel et al. 2016	Combined	Follow-up	0.180	0.254	0.064	-0.317	0.677	0.712	0.477
				0.179	0.124	0.015	-0.064	0.422	1.447	0.148

Hedges's g and 95% CI

-1.50   -0.75   0.00   0.75   1.50

Favours Control   Favours Treatment

Between group analysis for negative symptoms at post-treatment

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Hedges's g and 95% CI
Treatment vs control	Kim et al. 2010	Negative	Post treatment	0.280	0.357	0.128	-0.420	0.980	0.783	0.433	
Treatment vs control	Mueser et al. 2008	Negative	Post treatment	-0.050	0.468	0.219	-0.967	0.867	-0.107	0.914	
Treatment vs control	Mueser et al. 2015	Negative	Post treatment	-0.705	0.249	0.062	-1.193	-0.216	-2.827	0.005	
Treatment vs control	Steel et al. 2016	Negative	Post treatment	0.249	0.254	0.064	-0.248	0.747	0.981	0.327	
				-0.078	0.273	0.074	-0.613	0.456	-0.287	0.774	

Favours Control   Favours Treatment

Between group analysis for negative symptoms at follow-up

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Hedges's g and 95% CI
Treatment vs control	Kim et al. 2010	Negative	Follow-up	0.434	0.360	0.129	-0.271	1.139	1.206	0.228	
Treatment vs control	Mueser et al. 2008	Negative	Combined	0.399	0.480	0.230	-0.541	1.339	0.833	0.405	
Treatment vs control	Mueser et al. 2015	Negative	Follow-up	-0.211	0.242	0.059	-0.686	0.264	-0.870	0.384	
Treatment vs control	Steel et al. 2016	Negative	Follow-up	0.239	0.254	0.064	-0.259	0.736	0.941	0.347	
				0.122	0.156	0.024	-0.183	0.427	0.783	0.434	

Favours Control   Favours Treatment

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Between group analysis for delusions at post-treatment

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Treatment vs control	van den Berg et al. 2015	Delusions	Post treatment	0.594	0.177	0.031	0.247	0.941	3.353	0.001
Treatment vs control	Steel et al. 2016	Delusions	Post treatment	0.086	0.253	0.064	-0.409	0.582	0.341	0.733
				0.372	0.252	0.063	-0.121	0.866	1.479	0.139

Hedges's g and 95% CI

-1.50   -0.75   0.00   0.75   1.50

Favours Control   Favours Treatment

Between group analysis for delusions at follow-up

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Treatment vs control	van den Berg et al. 2015	Delusions	Follow-up	0.425	0.176	0.031	0.081	0.769	2.420	0.016
Treatment vs control	Steel et al. 2016	Delusions	Follow-up	0.291	0.254	0.065	-0.207	0.789	1.145	0.252
				0.382	0.144	0.021	0.099	0.665	2.642	0.008

Hedges's g and 95% CI

-1.50   -0.75   0.00   0.75   1.50

Favours Control   Favours Treatment

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Between group analysis for hallucinations at post-treatment

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Hedges's g and 95% CI
						Statistics for each study					
Treatment vs control	van den Berg et al. 2015	Hallucinations	Post treatment	0.492	0.263	0.069	-0.023	1.007	1.872	0.061	
Treatment vs control	Steel et al. 2016	Hallucinations	Post treatment	-0.208	0.254	0.064	-0.705	0.289	-0.820	0.412	
				0.139	0.350	0.122	-0.547	0.824	0.396	0.692	

-1.50   -0.75   0.00   0.75   1.50

Favours Control   Favours Treatment

Between group analysis for hallucinations at follow-up

Comparison	Study name	Outcome	Time point	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Hedges's g and 95% CI
						Statistics for each study					
Treatment vs control	van den Berg et al. 2015	Hallucinations	Follow-up	-0.153	0.260	0.068	-0.663	0.356	-0.591	0.555	
Treatment vs control	Steel et al. 2016	Hallucinations	Follow-up	0.021	0.253	0.064	-0.475	0.516	0.082	0.935	
				-0.064	0.181	0.033	-0.419	0.291	-0.353	0.724	

-1.50   -0.75   0.00   0.75   1.50

Favours Control   Favours Treatment

Secondary outcomes

Pre-post analyses found medium, significant effects on PTSD symptoms at both post treatment and follow up. However, in between-group analyses, effects were small at both post treatment and follow up and only met significance at follow up.

Both depression and anxiety symptoms showed small to moderate, significant effects at both time points in pre-post analyses, but had negligible, nonsignificant effects at both time points in between-group analyses.

9.6.4 Quality of outcomes

GRADE ratings for each outcome can be seen in Table 12. GRADE ratings indicated high confidence in between-group effect sizes for positive symptoms at both time points, delusions at follow up and PTSD at follow up. Issues with consistency and precision meant that other between-group outcomes were downgraded to varying degrees, most notably indicating very low or low confidence in between-group effect sizes for negative symptoms post treatment, hallucinations post treatment, and depression at both time-points.

9.6.5 Additional analyses

Heterogeneity

The majority of pre-post analyses showed moderate to high heterogeneity. In between-groups analyses, moderate to high heterogeneity was found for negative symptoms at follow up, and for delusions, hallucinations, PTSD, and depression at post treatment. Given this high level of heterogeneity, data entry was checked for error and moderator and sensitivity analyses conducted.

Moderator analysis

Therapy type, treatment length, and risk of bias were assessed as potential moderators in prespecified analyses. Study type (controlled vs uncontrolled) was also

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prespecified as moderator analysis, however this analysis was considered unnecessary since it was accounted for in the risk of bias moderator analysis.

Effects of interventions that included explicit exposure to the trauma memory (PE, written exposure, elements of imaginal exposure or EMDR) were compared with those that did not (cognitive restructuring interventions). In between-group analyses, PTSD symptoms at both post treatment and follow up were significantly moderated by therapy type (Q_1= 7.639, p= 0.006, Q_1= 5.619, p=0.018), with exposure-based therapies showing larger effects. There was also a trend towards positive symptoms post treatment (Q_1= 3.562, p= 0.059) and hallucinations post treatment (Q_1= 3.672, p= 0.055) being moderated by therapy type, again with exposure-based interventions showing larger effects, but this did not meet significance. In pre-post analyses, hallucinations at post treatment (Q_1= 4.262, p= 0.039) and negative symptoms at follow up (Q_1= 11.036, p= 0.001) were both significantly moderated by therapy type, with exposure-based therapies showing larger effects. Therapy type was not a significant moderator of any other outcomes.

Treatment length significantly moderated PTSD symptoms at post treatment in between-group analyses (β=-0.146, p= 0.002) and both positive and negative symptoms at follow up in pre-post analyses (β=-0.088, p= 0.02, β=-0.101, p= 0.02).

Risk of bias in individual studies did not significantly moderate any between-group outcomes but did significantly moderate negative symptoms at follow up (Q_1= 11.036, p= 0.001) and depression at follow up (Q_1= 8.185, p= 0.017) in pre-post analyses (studies with higher risk of bias showed larger effects).

Sensitivity analyses

Sensitivity analyses were conducted, involving: 1) removing the two studies that used active control groups (Bernard, 2006; Mueser et al., 2015) and, 2) adding the excluded 12 month time point from Mueser et al. (2015). These sensitivity analyses did not alter the significance or direction of any of the outcomes.

Calculation of fixed as opposed to random effects yielded no differences in results, other than for between-group analyses of delusions (g= 0.43, [0.71, 0.14] p= 0.003) and PTSD (g= 0.36 [0.59, 0.11] p= 0.003) at post treatment, both becoming significant.

9.7 Discussion

9.7.1 Summary of evidence

Primary outcomes: Do trauma-focused therapies have an effect on the symptoms of psychosis?

The results of the meta-analysis suggest that trauma-focused treatments have a small, significant effect on the positive symptoms of psychosis immediately following treatment. The between-group effect size of 0.31 post treatment is notable, since it is within the range of effect sizes usually reported for current best-practice CBT for psychosis when compared with TAU (Jauhar et al., 2014; van der Gaag et al., 2014; Wykes et al., 2008). However, the fact that this between-group effect was not maintained at follow up suggests that trauma-focused interventions in the form provided may not produce lasting changes. This may be an artifact of aspects of the treatment protocols used in included studies, for example the dose of treatment given, or, alternatively, may indicate that the initial positive effects found represent nonspecific treatment effects of trauma-focused interventions that are not maintained once treatment ceases. On a symptom level, similar magnitude between-group effects

were found for delusions, and this effect was significant at follow up. Again, between-group effect sizes in the magnitude of 0.38 are consistent with those found for current best practice treatments for delusions when compared with TAU (van der Gaag et al., 2014). Between-group analyses suggested no notable positive effects on either hallucinations or negative symptoms. This may suggest a symptom specific effect of trauma-focused treatments, consistent with the literature in the area, which has focused more on the relationship between positive symptoms of psychosis and PTSD, rather than negative symptoms. However, the limited effects on hallucinations are at odds with much of the literature that has suggested particular links between hallucinations and PTSD (Steel, 2015). Nonetheless, the analyses for delusions and hallucinations were limited by small numbers of studies.

Secondary outcomes: Can trauma-focused treatments be used to treat PTSD, anxiety and depression in people with psychosis?

The current meta-analysis did not find a significant between-groups effect of trauma-focused treatments on PTSD symptoms at post treatment, although finding a small, but significant effect on PTSD symptoms at follow up ($g = 0.31$). This is at odds with a recent meta-analysis that concluded that trauma-focused treatments are effective at treating PTSD in people with psychosis (Sin & Spain, 2016). This may be attributable to the Sin and Spain meta-analysis using a fixed effects model, whilst we had a priori chosen to use a random effects model due to the high degree of heterogeneity expected. Indeed, heterogeneity was moderate to high in between-group analyses of PTSD outcomes, supporting our analysis approach. Our results suggest that whilst there is some promise for trauma-focused treatments in treating PTSD in people with psychosis, further rigorous RCTs, are needed to confirm this. The

between-group results also suggest that trauma-focused treatments do not have a significant effect on symptoms of anxiety and depression in people with psychosis.

Which type of trauma-focused treatments show the best outcomes for people with psychosis?

Of interest, treatment modality was a significant moderator of PTSD outcomes, with exposure-based treatments showing greater effects. Exposure-based treatments appear to be a more fruitful avenue for future treatment and research than non-exposure based treatments. This finding is fitting with recent opinion in the area (Hardy & van den Berg, 2017). Treatment length also moderated some outcomes, however this is likely to be a function of treatment modality, since studies in this review that used exposure-based treatments offered less sessions than those not using exposure.

9.7.2 Limitations

The review yielded a small number of studies and many of these were at high risk of bias. The number of studies included in some analyses was small, particularly for hallucinations and delusions. Confidence in many of the findings was limited by issues with consistency and precision. Moderator analyses must also be interpreted with caution, since subgroups in these analyses were often small, meaning that the analyses lacked power.

The treatment signal found for PTSD in this review was relatively small, suggesting that trauma processing was not optimal in the treatments delivered. This limits conclusions regarding the role of trauma processing in improvements to psychotic symptoms. Indeed, it is of interest that treatment signals for psychotic symptoms were generally stronger than those for PTSD. However, caution should be

taken in interpreting differences in effect sizes for different outcomes given the small number of studies and overlapping confidence intervals for these effect sizes.

A key point when interpreting the results of this analysis is that the included studies were predominantly aimed at treating PTSD, meaning that trauma-focused work was specifically focused on index traumas for PTSD symptoms. This means that treatments were not tailored to target traumatic memories that may have been related to psychotic symptoms. There is notable individual variability in whether specific links can be found between a person's traumatic experiences and their psychotic symptoms (Hardy et al., 2005). The subgroup where links are strongest are likely to represent a particular target group for using trauma-focused interventions. Future research can focus on developing theoretically driven trauma-focused treatments for trauma-related psychotic symptoms for this subgroup, based on emerging literature in the area. The effects and mechanisms of action of these treatments can then be empirically tested (see Brand et al., 2017).

9.7.3 Conclusions

Overall, evidence for the impact of trauma-focused treatments on the symptoms of psychosis is small, but rapidly growing. Results here have shown some promising effects of trauma-focused treatments on positive symptoms of psychosis, however further development and evaluation of trauma-focused treatments for trauma-related psychotic symptoms is needed.

Chapter Ten: A Pilot Trial of Trauma-Focused Imaginal Exposure for Auditory Hallucinations (Peer Reviewed Publication Four).

10.1 Preamble to Publication Four

Publication Four is the first publication from Study Three and outlines the rationale, methods, and main quantitative findings of the pilot trial of trauma-focused imaginal exposure for auditory hallucinations. This study was the first study to specifically examine the feasibility, acceptability, and potential effects of a standard protocol, exposure-based trauma-focused intervention used specifically to treat trauma-related auditory hallucinations. This work built on the meta-analysis outlined in Chapter Nine by assessing the effects of a trauma-focused therapy that specifically targets the trauma memories deemed to be related to the auditory hallucinations, rather than just targeting traumatic memories related to PTSD symptoms (as in the majority of studies included in the meta-analysis). As such, this study allowed for additional insights into the potential of trauma-focused therapies in treating trauma-related auditory hallucinations.

Publication Four has been submitted and is currently under review for publication. The 'Author Indication Form', which details the nature and extent of the candidate and co-authors' contributions to this manuscript is included in Appendix VII. The candidate also convened a symposium at the World Congress for Behavioural and Cognitive Therapy (WCBCT) in Berlin in July 2019 titled 'using trauma-focused therapies to treat posttraumatic symptoms in psychosis: What works, when, and for whom?' and presented the findings from this publication as part of this symposium. The findings were also presented at the Early Career Hallucination Researcher (ECHR) annual meeting, Durham, 2019. The complete citations are as follows:

Brand, R.M., Bendall, S., Hardy, A., Rossell, S.L., and Thomas, N. (under review). A pilot trial of trauma-focused imaginal exposure for auditory hallucinations.

Brand, R.M., Bendall, S., Hardy, A., Rossell, S.L., and Thomas, N. (2019). A pilot trial of imaginal exposure therapy for people with trauma-related voices: results, lessons learnt, and questions to inform the development of trauma-focused therapies for psychosis. In, Bendall, S. (Chair) Using trauma-focused therapies to treat posttraumatic symptoms in psychosis: What works, when, and for whom? Symposium presented at the World Congress for Behavioural and Cognitive Therapies (WCBCT) conference, Berlin, Germany.

Brand, R.M., Bendall, S., Hardy, A., Rossell, S.L., and Thomas, N. (2019).

A pilot trial of trauma-focused imaginal exposure for auditory hallucinations. Open paper presentation at the Early Career Hallucination Researchers (ECHR) annual meeting, Durham, UK.

10.2 Abstract

Objective: There is mounting evidence that traumatic life events play a role in auditory hallucinations. Theory suggests that some auditory hallucinations are decontextualised trauma memory intrusions. Exposure-based trauma-focused therapies that target trauma memory intrusions may therefore be a promising new treatment. We aimed to assess the feasibility, acceptability, and potential effects of imaginal exposure for trauma-related auditory hallucinations.

Design: We conducted an uncontrolled pilot study of a six-session imaginal exposure intervention for trauma-related auditory hallucinations.

Results: Fifteen people were recruited to the trial and eligible to start the intervention. Participants reported high levels of satisfaction; however temporary distress and symptom exacerbation were common and contributed to discontinuation. There was a large reduction in auditory hallucination severity at one month follow up (adjusted d= 0.99), but individual response was highly variable. There were also large reductions in posttraumatic stress disorder symptoms, the intrusiveness of the trauma memory, and perceptual detail in the trauma narrative and medium reductions in negative posttraumatic cognitions.

Conclusions: Imaginal exposure for trauma-related auditory hallucinations is generally acceptable and may have large effects on auditory hallucination severity for some people. However, temporary distress and symptom exacerbation are common and can lead to discontinuation. Low referral rates and uptake also suggest feasibility issues for standalone imaginal exposure specifically for auditory hallucinations. The intervention may be more feasible and acceptable in the context of a broader trauma-focused therapy. Well-powered trials are needed to determine efficacy and identify factors that impact on acceptability and therapy response.

10.3 Key words

Trauma; Hearing voices; Auditory hallucinations; Trauma-focused; Imaginal exposure.

10.4 Practitioner points

- Some auditory hallucinations can be understood as trauma memory intrusions that lack temporal and spatial contextualisation and are therefore experienced without autonoetic awareness.

- Imaginal exposure to trauma memories associated with auditory hallucinations may be an effective intervention for some people.

- Temporary distress and symptom exacerbation may be common when using standard trauma-focused imaginal exposure for auditory hallucinations. This can impact on the acceptability of the therapy and should be considered in future development and delivery.

10.5 Background

Hearing a voice or noise in the absence of a corresponding external stimulus (variously termed 'auditory hallucinations', 'hearing voices', or 'voice-hearing') is a common experience for people meeting a range of diagnostic criteria (Larøi et al., 2012) and can lead to significant distress and disability. The current best-practice psychological treatment for psychosis, CBTp, has only shown small to moderate effects on auditory hallucinations (van der Gaag et al., 2014). To date, therapies for auditory hallucinations have largely been derived from empirical evidence relating to the importance of beliefs about auditory hallucinations in maintaining auditory hallucination-related distress (Chadwick & Birchwood, 1994); however there is growing evidence of other psychological processes that may be important in both the genesis and maintenance of auditory hallucinations, providing an opportunity for improving treatments (Thomas et al., 2014).

Posttraumatic psychological sequelae are increasingly recognised to have involvement in psychotic symptoms. There is mounting evidence that traumatic life-events are associated with psychotic symptoms and that this relationship is causal (Bailey et al., 2018; Kelleher et al., 2013; Varese et al., 2012). Theoretical models and empirical studies have implicated a range of posttraumatic processes in the specific relationship between trauma and auditory hallucinations (Williams et al., 2018).

One strand of this literature has focused on the role of trauma memory intrusions. Trauma memory intrusions are of interest due to their phenomenological

similarities with auditory hallucinations: both consisting of sensory experiences with no objective external stimulus and experienced as involuntary and (often) to represent a current threat (Morrison et al., 2003). The content of auditory hallucinations has direct or thematic links to trauma content in approximately 50% of people with auditory hallucinations who have experienced trauma (Hardy et al., 2005), suggesting that some auditory hallucinations may represent intrusions of traumatic memory material. Recently, Hardy (2017) has synthesised evidence in the area, theorising that one pathway from trauma to auditory hallucinations may be related to aspects of trauma memory encoding and retrieval that increase intrusions of trauma memories. Shifts in information processing during traumatic events result in episodic memories that are fragmented, decontextualised, and predominantly sensory-perceptual. This change in the encoding of episodic memory during traumatic events (termed *data-driven processing*) is central in contemporary theories of PTSD and contributes to re-experiencing symptoms (trauma memory intrusions and flashbacks; Brewin et al., 2010; Ehlers & Clark, 2000). Since psychosis is associated with impairments in spatial and temporal integration, it has been postulated that memories of traumatic events are more severely decontextualised in this group, leading to trauma memory intrusions that occur without autonoetic awareness and are therefore experienced as auditory hallucinations (Steel et al., 2005). These auditory hallucinations are characterised by content that includes direct replays of aspects of traumatic events (Hardy, 2017). Other posttraumatic psychological processes such as emotion regulation and negative posttraumatic beliefs are implicated in shaping these trauma memory intrusion-based auditory hallucinations and are also proposed as the basis of a second pathway from trauma to auditory hallucinations, likely characterised by

thematic, but not direct content links between auditory hallucinations and traumatic events (Hardy, 2017).

Trauma memory intrusions are targeted in well-evidenced psychological interventions for PTSD, including PE, trauma-focused CBT, and EMDR. Imaginal exposure, a central component of many of these interventions, encourages individuals to confront trauma memories in a controlled and safe environment. Proponents of PE hypothesise that fear habituation and reduction of negative posttraumatic beliefs are key mechanisms of change (Cooper, et al., 2017); however other models propose that imaginal exposure reduces intrusive trauma memories through elaboration and contextualisation of the memory (Brewin et al., 2010). Posttraumatic intrusions reduce in frequency, vividness and 'nowness' following imaginal exposure (Speckens et al., 2006).

Despite people with psychosis historically being excluded from trials of trauma-focused therapies, a recent trial has shown that a standard eight-session PE or EMDR intervention for comorbid PTSD is safe and effective in this population (van den Berg et al., 2015a, 2015b). A meta-analysis also indicated promising secondary effects of trauma-focused therapies on positive symptoms of psychosis (Brand, et al., 2017). Exposure-based trauma-focused therapies have been highlighted as a particularly potent treatment component for treating posttraumatic stress symptoms in psychosis (Hardy & van den Berg, 2017). Two recent case series have explored the effects of trauma-focused psychological interventions specifically targeting auditory hallucinations with some promising findings (Keen et al., 2017; Paulik et al., 2019). The treatment protocols in these studies did not have a central focus on trauma memory exposure but did include elements of this.

Given the putative role of trauma memory processing and intrusions in auditory hallucinations and indications that exposure-based trauma-focused therapies are particularly potent in targeting these processes, there is a strong rationale for the use of these therapies to treat distressing auditory hallucinations as a primary target. Large controlled trials are needed to assess the effectiveness of these approaches, and pilot effectiveness data will be important to inform the development of these trials. Despite the positive findings of the van den Berg (2015a) trial, potential issues with the use of trauma-focused approaches in psychosis have been highlighted, with clinicians reporting reluctance in delivery due to concerns about symptom exacerbation and safety (Gairns et al., 2015) and young people with a first episode of psychosis receiving a trauma therapy reporting distress and psychotic symptom exacerbation (Tong et al., 2017). Exploring the feasibility and acceptability of exposure-based trauma-focused therapies for distressing auditory hallucinations will therefore be important in determining whether more comprehensive assessments of efficacy are justified and whether any adaptations to the therapy are required.

10.6 Aims

We aimed to provide initial data on the feasibility and acceptability of trauma-focused imaginal exposure for people with trauma-related auditory hallucinations. We also aimed to provide estimates of effects on auditory hallucination severity and secondary symptom outcomes (PTSD, delusions, depression, and anxiety) as well as postulated mechanisms of change (trauma memory intrusions, the nature of the trauma memory, and posttraumatic cognitions).

10.7 Methods

10.7.1 Design

The Recall study was an uncontrolled pilot trial of a six-session imaginal exposure intervention for trauma-related auditory hallucinations. An independent researcher assessed outcomes at post treatment and one month follow up. The trial was prospectively registered as a pilot randomised-controlled trial (ACTRN: 12616001503415), but the trial design (and registration) was amended to an uncontrolled trial during the data collection phase due to slower recruitment than anticipated.

10.7.2 Participants

We invited people attending a specialist voices clinic and people on an auditory hallucinations research participant registry to take part in the study. We also promoted the study in local clinical services and consumer groups. Participants were required to (a) be aged 18-75; (b) have current auditory hallucinations (confirmed using item K6b of the MINI 7.02, Psychotic Disorders version; Sheehan et al., 1998) that were frequent and persistent (present for more than six months and occurring at least twice a week); (c) report a history of PTSD criterion A traumatic events, childhood adversity, or significant bullying; (d) have made some conceptual links between their past adverse experiences and their auditory hallucinations (e.g. direct content and indirect thematic links, including emotional and temporal associations) and, for this reason, be motivated to undertake a trauma-focused intervention and; (e) have a sufficient level of English language to participate in study requirements. Potential participants were excluded if (a) they had a recent (past month) or planned change in anti-psychotic medication; (b) they had substance-induced auditory hallucinations or current substance dependence issues that would interfere with

participation in the study; (c) they demonstrated acute risk to themselves or others, defined by the presence of suicidal or homicidal thoughts with current intent; (d) their treating team reported that undertaking the study treatment would pose a serious risk to the safety of the participant or other people; or (e) they had an estimated IQ<70 using the Wechsler Test of Adult Reading (Wechlser 2001).

10.7.3 Intervention

The imaginal exposure intervention was delivered over six weekly 90-minute sessions and was based on Foa's PE manual (Foa, Hembree, & Rothbaum, 2007). Imaginal exposure in PE involves exposure to the trauma memory for a prolonged time in sessions through repeated recounting of the trauma narrative and listening to audio recordings of this between sessions. The main adaptation to the PE imaginal exposure protocol for the present study was in the first session; in addition to standard education regarding PTSD symptoms, trauma memory processing, and avoidance, the therapist also spent time exploring links between traumatic events and auditory hallucination content.

In contrast to standard PE, in which the targeted trauma memories are those that are most intrusive, therapy targeted those recognised as having a link with auditory hallucinations. These were identified through collaborative formulation in the baseline assessment and session one of treatment. The trauma memories identified as the most representative of distressing auditory hallucination content, or that were most intrusive were prioritised for exposure work. Initial exposure sessions focused on a whole narrative of the traumatic event. Later exposure sessions were focused on memory 'hotspots' (i.e. those parts of the memory that seemed to represent the most distressing beliefs or emotions).

Therapy was delivered by a doctoral-level, registered clinical psychologist (10 years post qualification) with experience in trauma-focused therapies for PTSD and in psychological therapies for psychosis (RB) and supervised by a senior clinical psychologist with extensive experience in psychological interventions for auditory hallucinations (NT). Consultation regarding the therapy protocol and delivery was also provided by two specialists in the delivery of trauma-focused interventions for people with psychosis (SB and AH). An overview of therapy content is included in Table 16. Adherence to the therapy protocol was assessed by an independent researcher using a checklist of key elements for each session, with adherence of 95%.

10.7.4 Measures

Baseline participant characteristics

We used a self-report questionnaire to collect demographic information including age, gender, ethnicity, highest level of education, current psychiatric medication, and duration of auditory hallucinations.

Validated structured clinical interviews were used to assess for current psychotic or mood disorders (MINI 7.02, psychotic disorders version: Sheehan et al., 1998), borderline personality disorder (Structured Clinical Interview for DSM 5; First et al., 1997) and PTSD (Clinician Administered PTSD Scale for DSM-5, CAPS-5; Weathers et al., 2018).

Trauma history was confirmed and described using the Life Events Checklist for DSM-5 (Weathers et al., 2013b), the Childhood Trauma Questionnaire (Bernstein & Fink, 1998), and an item from the Trauma History Questionnaire (Hooper et al., 2011) assessing bullying.

At the end of the baseline interview we rated whether there was a direct relationship between participant's trauma exposure and auditory hallucination content

using criteria adapted from Hardy et al. (2005). This was done using up to three examples of participants' most distressing auditory hallucination content over the last week and details of the traumatic event from the CAPS-5. A direct relationship was operationalised as auditory hallucination content that included a literal correspondence to trauma content (i.e. auditory hallucination content included exact words, phrases, or sounds heard at the time of the trauma).

Feasibility and acceptability

Our assessment of feasibility and acceptability focused on uptake of and retention in the intervention. We recorded reasons for non consent, exclusion, or dropout throughout the study. Participants also completed the Client Satisfaction Questionnaire (Larsen, Attkisson, Hargreaves, & Nguyen, 1979) with an additional item measuring subjective improvement in auditory hallucinations.

Primary effectiveness outcome: Auditory hallucination severity

We assessed auditory hallucination severity using the Psychotic Symptoms Rating Scales – Auditory Hallucinations (PSYRATS-AHS; Haddock et al., 1999). Ecological momentary assessment (EMA) provided an additional measure of auditory hallucination intensity and distress. Ecological momentary assessment involves measurements at intervals throughout an individual's daily life and provides a sensitive, contextually valid measure that is less dependent on retrospective reporting. Participants were signalled to answer questions on a smartphone application, Movisens XS (https://xs.movisens.com), at ten pseudorandom time points each day for six days. The following questions were used: "Just before the beep went off I was hearing voices (that other people cannot hear)", [if 2 or above] "This was distressing" (rated on a scale of 1 to 7 where 1 = not at all, 4 = moderately and 7 = a lot). The items have previously been used in a psychosis population (Hartley et al., 2014).

Secondary effectiveness outcomes

PTSD symptom severity was assessed using the CAPS-5 (Weathers et al., 2013). The index trauma used for symptom severity ratings was the trauma identified as most related to the participant's auditory hallucination content. We assessed the severity of delusions using the Psychotic Symptom Rating Scales – Delusions Scale (PSYRATS-DS; Haddock et al., 1999) and depression and anxiety using the Depression Anxiety and Stress Scale–21 (DASS-21; Lovibond & Lovibond, 1995).

Mechanisms of change

Trauma memory intrusion intensity and distress were measured as part of the EMA schedule using the items: "Thinking about the traumatic or stressful event(s) we identified as related to your voices… since the last beep, memories of the event(s) came into my head when I did not want them to", [if 2 or above] "This was distressing". We used the Trauma Memory Questionnaire (TMQ; Halligan et al., 2003) to assess the intrusiveness and disorganisation of the trauma memory. We also assessed the extent to which memories were encoded in a sensory-perceptual or a semantic (cognitive) form by analysing trauma narratives from participants' first and final imaginal exposures using Linguistic Inquiry and Word Count (LIWC; Pennebaker, Boyd, Jordan, & Blackurn, 2015), calculating the percentage of words classified as 'perceptual' (e.g., see, hear) and 'cognitive' processes (e.g. cause, maybe, know). Negative posttraumatic cognitions were assessed using the Posttraumatic Cognitions Inventory (PTCI; Foa, Ehlers, Clark, Tolin, & Orsillo, 1999).

Session by session data

Participants rated auditory hallucination and trauma memory intrusion frequency and distress over the previous week on a scale of 0 to 10 at the beginning of each therapy section.

Distress, symptom exacerbation and adverse events

Participants who completed therapy rated how much distress they had experienced during their sessions. Additionally the session-by-session ratings (described above) captured symptom exacerbation during therapy. Serious adverse events were recorded throughout the study.

10.7.5 Statistical analysis

Feasibility and acceptability results are reported descriptively. Our preregistered analysis plan for effectiveness outcomes included significance testing using repeated measures analysis of variance and paired t-tests; however, our final sample size meant that these tests would have been underpowered. In line with recommendations for pilot trials (Leon et al., 2011) and our aim to provide estimates of effects, we therefore only examined effect sizes and 95% confidence intervals. Effect sizes between baseline and one month follow up were calculated as M_{pre}-M_{post}/SD_{pre} and adjusted for unbiased d (Lakens, 2013). Effect sizes for non-normal variables were calculated as $r = z/\sqrt{(n)}$ (Rosenthal, 1991) and then converted to unbiased d.

In addition to these preregistered analyses, we visually inspected session-by-session data to describe trends in mean scores. We also divided the sample into those with a direct trauma- auditory hallucination content link and those without to examine whether these groups had different treatment response.

10.8 Results

10.8.1 Participant characteristics

Fifteen people were in the final study sample. Basic demographic and clinical characteristics of participants at baseline are shown in Table 13.

Table 13. Participant demographics: Study Three (*n* = 15).

Age, m (SD)	43.79 (8.64)
Gender, *n* (%)	
Female	9 (60.00)
Male	5 (33.34)
Other	1 (6.67)
Ethnicity, *n* (%)	
Caucasian	13 (86.67)
Hispanic	1 (6.67)
Other	1 (6.67)
Highest level of education, *n* (%)	
Primary	1 (6.67)
Secondary	2 (13.33)
Tertiary	12 (80.00)
Index traumatic event type, *n* (%)	
Childhood sexual abuse	3 (20.00)
Childhood physical abuse	2 (13.34)
Childhood emotional abuse	4 (26.67)
Adulthood sexual abuse	5 (60.00)
Bullying	1 (6.67)
Workplace accident	1 (6.67)
Witnessing death of family member	1 (6.67)
Military trauma	1 (6.67)
Primary diagnosis, *n* (%)	
Schizophrenia spectrum disorder	10 (66.67)
Mood disorder with psychotic features	4 (26.67)
Borderline personality disorder	1 (7.67)
Comorbid PTSD, *n* (%)	6 (40.00)
Comorbid BPD, *n* (%)	3 (20.00)
Number of years had AH, m (SD)	19.17 (10.67)
Taking anti-psychotic medication, n (%)	
Yes	11 (73.00)
No	3 (20.00)
Missing	1 (6.67)

Note. AH = auditory hallucinations, BPD = borderline personality disorder, m = mean, n = number of participants, PTSD = posttraumatic stress disorder, SD = standard deviation.

10.8.2 Uptake

Fifty-six people were screened for eligibility. Twenty-four people did not want to do a trauma-focused therapy. Two declined participation on their treating clinician's advice and two were not able to travel to the sessions. Ten people did not meet inclusion criteria: no trauma history (n=5), no current auditory hallucinations (n=4), intellectual disability (n=1), already receiving a trauma-focused therapy (n=1). Seventeen people were eligible and consented to take part. Two of these participants had to be withdrawn from the study at the baseline assessment stage (one due to substance use, and one on the advice of their treating team who had safety concerns).

The study was initially designed and registered as a pilot randomised controlled trial. We predicted a recruitment rate of two people per month, based on recruitment to previous auditory hallucination therapy trials run locally. However we recruited on average one person per month. As such, a 'stop rule' was initiated after eight months of recruitment, and the trial switched to an uncontrolled pilot trial.

10.8.3 Retention

Fifteen people were enrolled to receive the study therapy. One participant was not contactable following the baseline assessment and did not begin the therapy. Of the 14 participants who did start the therapy, 11 completed all six sessions. One participant ceased therapy after two sessions due to distress and symptom exacerbation but was willing to complete the follow up assessments. One participant ceased therapy after four sessions due to distress and symptom exacerbation and did not want to participate in follow up interviews. Another participant ceased therapy after two sessions due to an acute mental health inpatient admission (deemed unrelated to participation in the study by the participant and her treating psychiatrist) and was unable to complete follow up assessments.

10.8.4 Satisfaction

All participants who completed the satisfaction survey (*n*=12) rated the quality of the treatment as excellent and that they were satisfied with the treatment (66.7% 'very satisfied', 33.3% 'mostly satisfied). All participants reported that they would recommend the therapy to a friend who was in need of similar help (66.7% 'yes definitely', 33.3% 'yes, I think so') and that the therapy sessions helped them to deal more effectively with their problems (58.3% 'yes, they helped', 41.7% 'yes, they helped a great deal'). Participants generally reported that their needs had been met by the therapy (58.3% 'most of my needs have been met', 25.0% 'almost all of my needs have been met), however 16.7% reported that only a few of their needs had been met. Over half of participants reported that their auditory hallucinations were improved following the therapy (50.0% 'voices are better', 8.3% 'voices are much better'), but 25.0% reported no change in their auditory hallucinations and 8.3% that their auditory hallucinations were worse.

10.8.5 Primary effectiveness outcome: auditory hallucinations severity.

Mean reduction in the PSYRATS-AHS was 3.5 points (95% CI -10.59, 3.59) at post treatment and 8.5 points (95% CI -17.31, 0.31) at follow up (see Table 14), representing a large standardised effect size at this timepoint (adjusted $d = 0.99$). However, there was large variance in individual participant outcomes. Notably, two participants had total remission from their auditory hallucinations at follow up.

EMA data showed reductions of a small magnitude in mean auditory hallucination intensity and medium magnitude for auditory hallucination-related distress.

Table 14. Outcomes measured at baseline, post treatment and follow up: Study Three (*n*=12).

Outcome	Baseline		Post		Follow up		Mean difference baseline-post (95% CI)	Mean difference baseline-follow up (95% CI)	ES
	M	SD	M	SD	M	SD			
PSYRATS-AHS	29.58	7.96	26.08	11.04	21.08	12.94	-3.50 (-10.59, 3.59)	-8.50 (-17.31, 0.31)	0.99
CAPS-5	26.75	14.89	15.17	11.38	11.92	10.54	-11.58 (-22.20, -0.96)	-14.83 (-25.97, -3.70)	0.93
PSYRATS-D$^\$$	5	18.25	0.00	15.25	0.00	10.50	0.00 (-2.00, 0.00)	0.00 (-10.00, 1.00)	0.56
DASS Depression	10.25	6.14	8.25	5.50	8.00	5.51	-2.00 (-5.93, 1.93)	-2.25 (-5.87, 1.37)	0.34
DASS Anxiety	8.17	4.13	6.17	4.22	5.50	4.44	-2.00 (-5.56, 1.56)	-2.67 (-6.03, 0.70)	0.60
TMQ intrusiveness	2.48	1.04	1.66	1.15	1.29	0.92	-0.82 (-1.47, -0.18)	-1.19 (-1.78, -0.59)	1.06
TMQ disorganisation	1.32	1.12	1.42	1.08	1.40	1.29	0.10 (-1.01, 0.81)	0.08 (-1.11, 0.94)	0.07
PTCI	136.33	36.20	114.75	45.72	107.83	50.89	-21.58 (-43.79, 0.62)	-28.50 (-54.87, -2.13)	0.73

Note. ES (adjusted *d*) reported for change between baseline and follow up. $^\$$ variable not normally distributed: median values (inter quartile range), and median change (CI) reported. CAPS-5 = Clinician Administered PTSD Scale for DSM-5, CI = confidence interval, DASS = Depression Anxiety and Stress Scale, ES = effect size, M = mean, PSYRATS-AHS = Psychotic Symptom Rating Scales-Auditory Hallucination Scale, PSYRATS-DS = Psychotic Symptom Rating Scales-Delusions Scale, PTCI = Posttraumatic Cognitions Inventory, SD = standard deviation, TMQ = Trauma Memory Questionnaire.

Table 15. Outcomes measures at baseline and post treatment: Study Three (n=12).

Outcome	n	Baseline		Post		Mean difference baseline-post	
		M	SD	M	SD	(95% CI)	ES
AH intensity	10	3.50	1.89	3.34	1.94	-0.16 (-0.98, 0.66)	0.08
AH distress	10	4.37	0.74	3.78	1.52	-0.60 (-1.39, 0.19)	0.74
Intrusion intensity	10	2.65	1.44	2.45	1.39	-0.19 (-1.23, 0.85)	0.13
Intrusion distress	10	4.20	1.20	3.16	1.65	-1.04 (-2.34, 0.26)	0.81
Perceptual detail in trauma narrative[$]	11	3.45	0.98	2.67	1.19	-0.32 (-2.21, 0.47)	1.28
Cognitive processing in trauma narrative	11	10.04	3.83	10.63	4.39	0.58 (-1.76, 0.59)	0.14

Note. ES (adjusted *d*) reported for change between baseline and follow up. [$] variable not normally distributed: median values (inter quartile range) and median change (CI) reported. AH = auditory hallucination, CI = confidence interval, ES = effect size, n = number of participants, M = mean, SD = standard deviation.

10.8.6 Secondary effectiveness outcomes and mechanisms of change

Results for secondary outcomes and mechanisms of change are detailed in Table 14 and Table 15. There was a large, consistent reduction in PTSD symptom severity at one month follow up (adjusted d = 0.93). EMA measures of trauma memory intrusions showed reductions of a small magnitude for mean intensity and a large magnitude for mean distress. Reductions in delusions, depression, and anxiety were small to medium.

There were medium to large changes in the intrusiveness of the trauma memory (adjusted d = 1.06) the level of perceptual detail in the trauma narrative (adjusted d = 1.28), and negative posttraumatic cognitions (adjusted d = 0.73 at one month follow up). Reductions in the disorganisation of the trauma memory and increases in cognitive processing in the trauma narrative were minimal.

10.8.7 Session-by-session data

Visual inspection of mean session-by-session auditory hallucination and trauma memory intrusion frequency and distress scores (n=11 treatment completers, shown in Figure 6.) shows a downward trend over the six sessions. When the sample were divided into those who had a direct link between the content of their auditory hallucinations and the trauma (n=3, Figure 7a.), and those who did not (n=8, Figure 7b.) plots are suggestive of differing trajectories of treatment response, with those with a direct link showing larger changes.

Figure 6. Study Three: Mean session-by-session ratings of auditory hallucination and trauma memory intrusion frequency and distress (*n* =11).
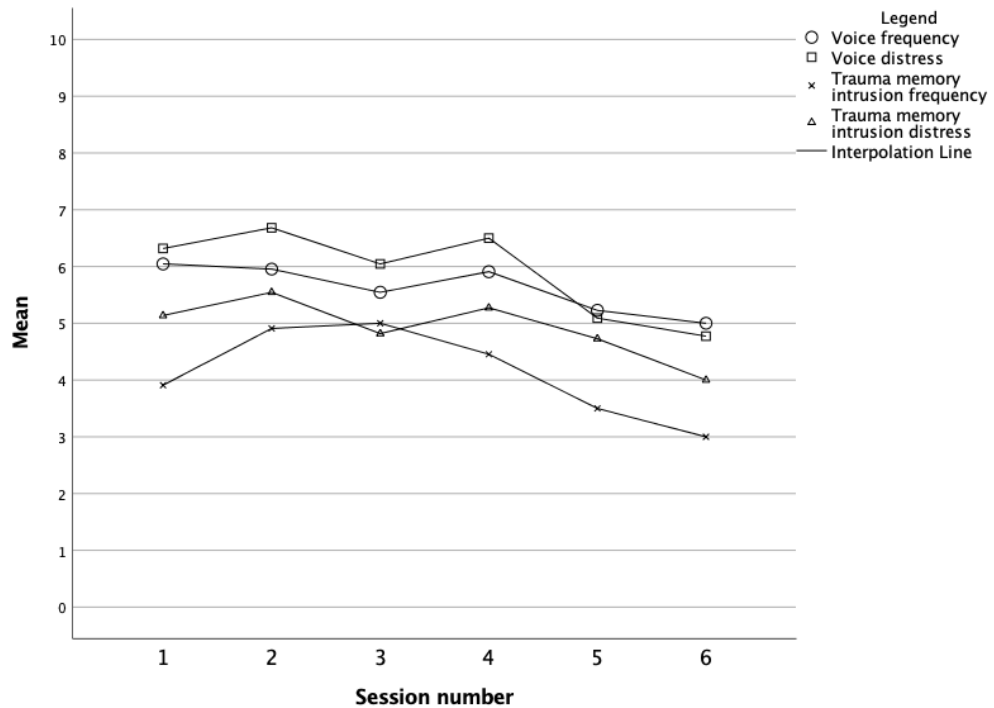
Figure 7. Study Three: Mean session-by-session ratings of auditory hallucination and trauma memory intrusion frequency and distress in those with a direct auditory hallucination-trauma content link (*n*=3, a) and those without (*n*=8, b).

a)
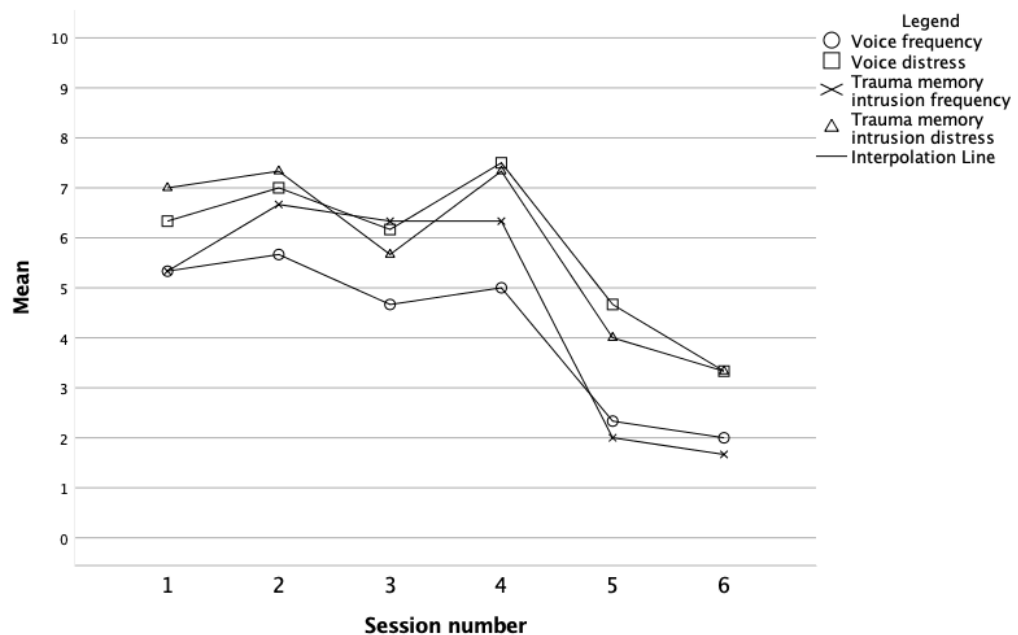
b)
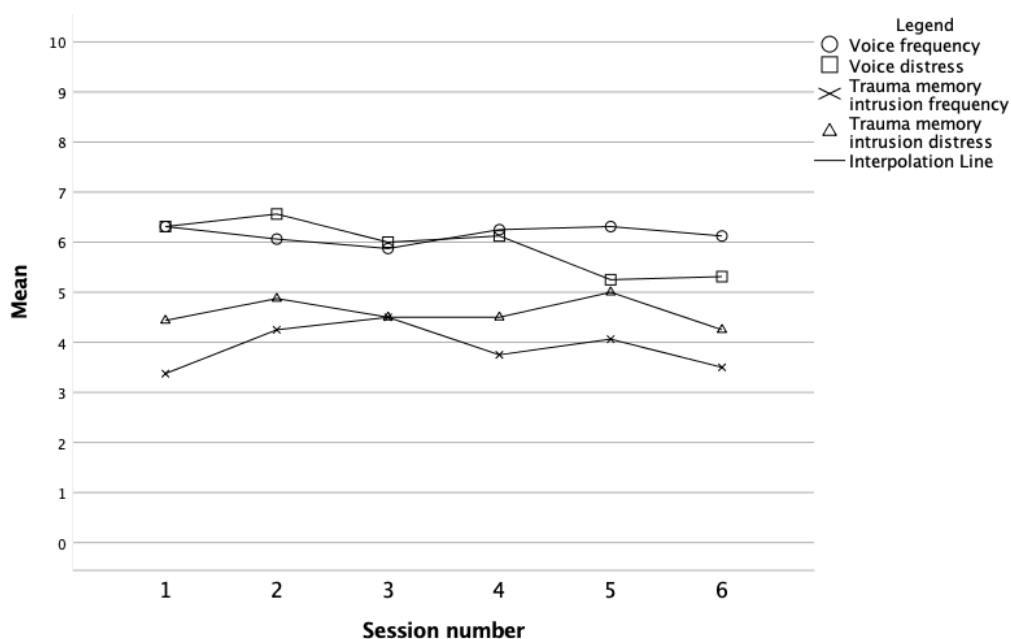
10.8.8 Distress, symptom exacerbation and adverse events

All participants who completed the satisfaction survey (*n*=12) reported some level of distress in their sessions: 66.7% reported moderate distress that they felt able to manage and 25.0% reported experiencing severe distress that they did not feel able to manage.

Visual inspection of mean session-by-session scores (Figure 6.) is suggestive of a slight exacerbation of trauma memory intrusions and auditory hallucinations between session one and two and between session three and session four.

Three participants had mental health-related inpatient admissions during the study. None of these admissions were deemed to be related to study participation (one admission prior to commencement of therapy for withdrawal from benzodiazapines, one admission between post treatment and follow up for electroconvulsive therapy, one admission for suicidal ideation that both the participant and psychiatrist reported to be unrelated to participation in the study). Of note, two participants did discontinue therapy sessions and reported increased distress and

exacerbation of PTSD and auditory hallucinations as a reason for this. One of these participants agreed to a follow up assessment, at which point their symptoms had returned to baseline levels.

10.9 Discussion

The Recall study is the first study to examine the feasibility, acceptability, and potential effects of an exposure-based trauma-focused therapy, imaginal exposure, for trauma-related auditory hallucinations. Our findings suggest promising effects for some auditory hallucinations, but also highlight some potential feasibility and acceptability issues in delivering this standard exposure-based trauma focused therapy specifically for trauma-related auditory hallucinations.

10.9.1 Is imaginal exposure a feasible treatment for trauma-related auditory hallucinations?

Previous research has suggested that delivering standard exposure-based trauma-focused therapies to treat PTSD in people with psychosis is feasible (van den Berg et al., 2015a), but the findings of the present study have highlighted some potential feasibility issues when delivering these therapies specifically to treat trauma-related auditory hallucinations. Referral and uptake rates for this study were low, despite the study being advertised widely. The prevalence of traumatic events is known to be high in people with auditory hallucinations, and there is indication that many people identify their trauma history to be of importance in their auditory hallucinations (Corstens & Longden, 2013). We would therefore speculate that the reason for low referral and uptake does not reflect low demand for trauma therapies, but is perhaps related to perceptions of exposure-based trauma-focused therapies specifically. Indeed, clinician reluctance to undertake these therapies is well documented in PTSD treatment literature (Becker et al., 2004) and in psychosis

(Gairns et al., 2015). Further research into clinician and client perspectives of exposure-based trauma-focused therapies for auditory hallucinations is warranted. Because we were interested in testing the effects of exposure-based trauma-focused therapies as a standalone intervention, we required participants to have already made links between their auditory hallucinations and past trauma (so that exposure to identified trauma memories could commence in session two). This may be another reason for low referral and uptake rates. Many clinical services traditionally have an emphasis on biomedical explanations of auditory hallucinations, meaning that many clinicians and clients in the mainstream health system may not have developed a trauma-informed understanding of auditory hallucinations, possibly reducing the likelihood of uptake of a trial of this nature. To increase feasibility, exposure-based trauma-focused interventions for auditory hallucinations may need to be delivered as a component of a broader trauma-informed treatment in which links between auditory hallucinations and trauma can be formulated over time and trust in the rationale for exposure-based trauma-focused therapies developed.

10.9.2 Is imaginal exposure an acceptable treatment for trauma-related auditory hallucinations?

Participants who completed therapy reported high levels of satisfaction, despite the brief nature of the therapy and the use of trauma memory exposure early in treatment. The rate of dropout from therapy (26.7%) was relatively high in relation to some psychological treatment trials for auditory hallucinations (e.g. Birchwood et al., 2014, 12.2%; Hazell et al., 2018, 14.3%), but in line with others (Craig, Ward, & Rus-Calafell, 2016, 29.3%). Van den Berg also reported a therapy dropout rate of 22.0% when using trauma-focused therapy for PTSD in psychosis populations (van den Berg et al., 2015a) and dropout from trauma-focused therapies in general PTSD

populations is 20-27% (Hembree et al., 2003). This suggests that imaginal exposure

for trauma-related auditory hallucinations may be as acceptable as other related

therapies. Importantly, participants who dropped out of the current therapy cited

increased levels of distress and exacerbation of auditory hallucinations and PTSD

symptoms that were too difficult to tolerate. Indeed, 25.0% of therapy completers also

reported severe distress that they did not feel able to manage during the sessions.

Session-by-session data was also suggestive of a small exacerbation in auditory

hallucinations and trauma memory intrusions in early sessions that then decreased as

sessions progressed. This is in contrast with the large trial of PE and EMDR for

comorbid PTSD in people with psychosis, which did not find exacerbation of

psychotic or PTSD symptoms (van den Berg, 2015a). This difference may be an

artefact of the different focus of therapy in the present study (trauma-related auditory

hallucinations rather than PTSD), or to differences in participant characteristics or

their service contexts. Only 40% of participants in van den Berg's (2015a) study had

active auditory hallucinations, whereas all participants in this study had current

persistent and distressing auditory hallucinations. It is possible that distress and

symptom exacerbation are more pertinent when working with trauma that is

associated specifically with active psychotic symptoms. The tension between

undertaking trauma memory exposure work and managing distress is inherent in all

trauma-focused therapies and there has been much debate regarding the need for a

'stabilisation' phase prior to memory exposure work, particularly in people with

complex trauma histories and symptoms (De Jongh et al., 2016). The results here

suggest that when treating trauma-related auditory hallucinations, most people are

able to tolerate trauma-memory exposure work without stabilisation, but a number of

people may benefit from a stabilisation phase prior to exposure work. It will be

important to develop our understanding of clinical and contextual factors that influence the tolerability of exposure-based trauma-focused therapies for different people.

10.9.3 What are the potential effects of imaginal exposure on trauma-related auditory hallucinations?

We estimated a large effect of imaginal exposure on auditory hallucination severity, however individual participant changes were variable. With the small sample, confidence intervals around mean change scores were wide, so cannot rule out a null hypothesis of no effect. Two clients experiencing complete remission from auditory hallucinations is notable given the chronicity of these experiences in our sample. Instances of complete remission from auditory hallucinations have also been reported in other studies using trauma-focused approaches for people with auditory hallucinations (van den Berg & van der Gaag, 2012; Paulik et al., 2019) and may suggest that it is a particularly effective treatment for some people. Ecological momentary assessment measures used as an additional measure of auditory hallucinations produced larger effect size estimates for auditory hallucination-related distress than for auditory hallucination intensity. However, the large overlap between confidence intervals, and fact that EMA data were only available at post treatment should be noted. Clinical observations during this trial led us to hypothesise that the treatment was particularly potent for a small group of people whose auditory hallucinations included exact replays of traumatic material (e.g. an abuser making threats). In a supplementary analysis we therefore separated the sample (direct vs no direct auditory hallucination-trauma content link) and visually inspected differences in trajectories of session-by-session scores. The plots do indicate a larger treatment response for those with these 'direct' auditory hallucination-trauma content links.

However, larger, well-powered studies are needed to more definitively examine efficacy and contextual and clinical factors that moderate treatment response.

10.9.4 What are the likely mechanisms of action in imaginal exposure for trauma-related auditory hallucinations?

Posttraumatic stress symptoms showed large reductions over the course of treatment. The effects seen here are in line with those from previous studies (van den Berg et al., 2015a) and suggest that participants received a sufficient 'dose' of imaginal exposure to act on the mechanisms of interest. The imaginal exposure did indeed have large effects on the intrusiveness of the trauma memory and perceptual detail in the trauma narrative. This suggests that the therapy did impact on some aspects of the nature of the trauma memory, a key hypothesised mechanism of interest. However, there were minimal effects on the disorganisation and cognitive processing of the memory. There were also medium effects on negative posttraumatic beliefs, which, although not directly targeted, are in line with other studies of PE (Cooper et al., 2017).

Trauma memory processing is particularly implicated as a psychological mechanism in auditory hallucinations that represent direct replays of trauma content (Hardy, 2017). Our observation that people with direct content links may have had a better response to imaginal exposure is in keeping with this theory, suggesting that trauma memory processing is particularly involved in this type of auditory hallucinations and that treatments specifically addressing this are more potent for this group. However, it must be noted that our findings were also suggestive of changes in negative posttraumatic beliefs being a mechanism of action in imaginal exposure, suggesting that imaginal exposure acts on multiple mechanisms. As a small pilot

study, these interpretations are also speculative. The mediating effects of mechanisms of interest will need to be examined in larger, well-powered trials in the future.

10.9.5 Strengths and limitations

To our knowledge, this is the first study to specifically test the effects of imaginal exposure for trauma-related auditory hallucinations. As such the study provides novel data on the feasibility, acceptability, and potential effects of this approach. However, the small sample size limits conclusions regarding efficacy due to low power to detect effects. Similarly, the lack of a control group means that the specific effects of the intervention cannot be disentangled from natural changes in symptoms over time and from nonspecific therapy effects. The study also recruited a very specific group of participants (i.e. those who had already made links between their auditory hallucinations and their trauma history). The findings found here therefore provide a 'proof of concept' that this intervention *can* have some positive effects on auditory hallucinations, but a large well-powered randomised controlled trial is needed to definitively assess efficacy.

10.10 Conclusions

Imaginal exposure for trauma-related auditory hallucinations can have large effects on auditory hallucination severity, but individual response is highly variable. Some people may find the process of exposure difficult to tolerate. Further research is needed to definitely assess efficacy and to identify clinical and contextual factors that influence therapy response and tolerability.

Chapter Eleven: A Tale of Two Outcomes: Remission and Exacerbation in the Use of Trauma-Focused Imaginal Exposure for Trauma-Related Voice-hearing. Key Learnings to Guide Future Practice (Peer Reviewed Publication Five).

11.1 Preamble to Publication Five

Publication Five is the second publication from Study Three. The experience of delivering the intervention in this study led to important clinical insights and hypothesis generation regarding contextual and individual factors that might influence the tolerability and effectiveness of these therapies. It was not possible to convey this rich individual level information in detail in the main quantitative findings of Publication Four, so Publication Five aimed to outline some of these insights through the presentation of two case illustrations. Both of the participants described in Publication Five used the terms 'voices' or 'voice-hearing' to describe their experience, so this terminology was used throughout the manuscript (rather than the term 'auditory hallucinations' that has been used throughout the rest of the thesis).

Publication Five has been accepted for publication and is in press in the journal *Clinical Psychologist*, which is a journal of the Australian Psychological Society with a focus on bridging the gap between clinical research and clinical practice. The 2018 impact factor for *Clinical Psychologist* was 1.29. The 'Author Indication Form', which details the nature and extent of the candidate and co-authors' contributions to this manuscript is included in Appendix VIII. The complete citation is as follows:

Brand, R.M., Hardy, A., Bendall, S., and Thomas, N. (in press). A tale of two outcomes: Remission and exacerbation in the use of trauma-focused imaginal

exposure for trauma-related voice-hearing. Key learnings to guide future practice.

Clinical Psychologist.

11.2 Abstract

Objective: Many people who hear voices (also termed auditory-verbal hallucinations) have experienced traumatic or adverse life events. There is growing evidence that, for a number of people, these events are an important contributing factor to voice-hearing experiences. Psychological mechanisms implicated in the trauma-voice-hearing relationship overlap with those involved in posttraumatic stress disorder, giving a strong rationale for the use of exposure-based trauma-focused therapies for distressing voices. There is currently limited clinical guidance in this area and, despite preliminary evidence of effectiveness, clinicians report reluctance to deliver these therapies. We believe that two key questions will be important in informing the delivery of exposure-based trauma-focused therapies for distressing voices; namely, what influences their acceptability and tolerability, and who is most likely to benefit?

Method: We present two case illustrations from an ongoing pilot trial in which people with trauma-related voices received six sessions of imaginal exposure.

Results: Tara and Laura had very different therapy outcomes and we believe their experiences provide some initial insights into processes and factors that may impact on the delivery of exposure-based trauma-focused therapies for voice-hearing.

Conclusions: We highlight the potential for symptom exacerbation in early sessions and consider how this might influence acceptability, including the possibility that exposure therapy may be less tolerable when clients have persecutory appraisals of their voice-hearing experience. We also explore the potential therapeutic

importance of associations between trauma and voices, suggesting exposure therapy is particularly indicated when there is a direct link between the content of voices and the index trauma.

11.3 Key words: exposure, hallucinations, hearing voices, psychosis, trauma, trauma-focused.

Key points

- Many people who hear voices have experienced traumatic events and posttraumatic sequelae may contribute to voices.
- Trauma-focused imaginal exposure may be helpful for people with trauma-related voice hearing experiences, particularly those with a direct link between the content of their voices and their index traumatic event.
- There is potential for symptom exacerbation in early sessions of exposure-based trauma-focused therapies for distressing voices this should be considered when planning exposure work and should be monitored throughout therapy.

11.4 Introduction

Hearing a voice in the absence of a corresponding external stimulus (variously termed 'auditory verbal hallucinations', 'hearing voices', or 'voice-hearing') is a common experience for people meeting a range of diagnostic criteria (including schizophrenia spectrum disorders, mood disorders, borderline personality disorder, and PTSD) and is often associated with significant distress. Research suggests that multiple bio-psycho-social processes are involved in the formation and maintenance of voices.

In recent years there has been an increasing interest in the role of trauma and posttraumatic sequelae in voice-hearing. There is now compelling evidence that traumatic life-events are associated with psychotic symptoms, including voice-hearing (Varese et al., 2012), and that this association may be causal (Kelleher et al., 2013).

It is apparent that not all voice-hearing experiences are related to trauma (Luhrmann et al., 2019); however, the content of voices bears a meaningful relationship to traumatic life-events for a large proportion of people. Within a sample of voice-hearers with a trauma history, it was found that 13% had a literal content link, and 45% had a thematic link between their voices and trauma (Hardy et al., 2005). This group may represent those for whom trauma is particularly relevant.

Hardy (2017) reviews evidence indicating two different pathways from trauma to voice-hearing, with episodic memory, negative schematic beliefs, and emotion-regulation strategies differentially implicated in each pathway (see Williams et al., 2018 for an in-depth synthesis of this literature). Firstly, some trauma-related voices may be a form of posttraumatic intrusion that is particularly decontextualised and fragmented and is therefore not recognised to be a memory but experienced as a current external threat. The development and maintenance of these voices is primarily linked to the encoding and retrieval of episodic memories, with emotional regulation and beliefs also playing a role. At times of extreme emotion (such as in traumatic events), shifts in information-processing can lead to vivid, fragmented, sensory-perceptual memories that are vulnerable to intruding into consciousness. These changes in the encoding of memories during traumatic events (termed 'data-driven' processing) are central in contemporary theories of PTSD and are thought to contribute to posttraumatic intrusions and flashbacks (Brewin et al., 2010; Ehlers & Clark, 2000). As psychosis is associated with impairments in spatial and temporal

integration, it has been suggested this may account for even more severe decontextualisation, such that an intrusion is experienced without any autonoetic recollection (Steel et al., 2005).

In contrast, the second pathway proposes that some voices are not directly linked to episodic memory, but instead represent auditory images (or anomalous experiences). These voices have indirect links to trauma as their content and appraisals are shaped by beliefs about the self and others abstracted from traumatic events and stored in autobiographical memory. They are also influenced by regulation strategies developed as survival mechanisms during trauma, such as dissociation, avoidance, and hypervigilance, given the impact of these processes on sensory-perceptual processes.

Notably, the posttraumatic mechanisms implicated in both hypothesised pathways to voice hearing are also associated with the development of PTSD (Brewin et al., 2010; Ehlers & Clark, 2000; Foa & Kozak, 1986) and are the targets of well-evidenced psychological interventions for PTSD (PE, trauma-focused CBT, and EMDR). The significant overlap in the phenomenology and psychological mechanisms involved in trauma-related voices and PTSD provides a clear rationale for the application of trauma-focused therapies (well established in their effectiveness for PTSD) in treating distressing voices. Despite people with psychosis historically being excluded from trials of trauma-focused therapies, recent trials have shown positive effects on PTSD in this population, as well as indicating the safety of using such interventions (e.g. van den Berg et al., 2015a, 2015b). Our recent meta-analysis also showed that trauma-focused treatments in these trials have promising effects on positive symptoms of psychosis, though this has generally been examined as a secondary outcome (Brand, et al., 2017).

There is growing interest in the application of trauma-focused therapies specifically targeting trauma-related voice-hearing. Two recent case series included aspects of exposure to voice-related trauma memories in their treatment protocols, with encouraging results (Keen et al., 2017; Paulik et al., 2019). Despite the growing interest in the area, there remains limited guidance for clinicians in the delivery of trauma-focused therapies for trauma-related psychotic symptoms. Guidance does exist regarding the conceptualisation and treatment of trauma-related psychotic symptoms with EMDR (van den Berg, van der Vleugel, Staring, de Bont, & de Jongh, 2013) but there is little information to guide clinical practice using other trauma-focused approaches. Guidance in the use of exposure-based trauma-focused therapies is perhaps particularly important. Despite indications that these therapies may be the most potent in addressing posttraumatic symptoms in psychosis (Hardy & van den Berg, 2017), in practice, they are rarely delivered due to clinician concerns about safety and tolerability (Gairns et al., 2015). In order to increase the delivery of acceptable and effective exposure-based trauma-focused therapies for trauma-related psychotic symptoms we believe guidance is needed regarding two main questions– what factors impact on their acceptability and tolerability, and who is most likely to benefit?

As part of our research programme in this area, we are conducting a pilot-trial of a trauma-focused therapy component (imaginal exposure) for trauma-related voice-hearing (ANZCTR: 1261600150341), with quantitative and qualitative findings forthcoming. Our experience of delivering therapy in this trial has led to some insights that we believe may provide some tentative guidance in relation to the delivery of trauma-focused therapies for psychosis. In this paper we will illustrate

these insights through comparing and contrasting the experiences of two participants (Tara and Laura) who had very different responses to therapy.

11.5 Methods

11.5.1 Intervention

Tara and Laura were both offered six-sessions of trauma-focused imaginal exposure based on Foa's PE manual (Foa et al., 2007). PE is a specific cognitive behavioural therapy in which clients are supported to approach (rather than avoid) trauma-related memories, emotions, and situations. We chose to use the PE protocol because it has, arguably, the best evidence base for treating PTSD symptoms. Additionally, PE is one of the only trauma-focused therapies that has so far been studied in a large trial in a psychosis population (van den Berg et al., 2015a). We chose to deliver only the imaginal exposure aspects of the therapy because we were particularly interested in the impact of elaborating and contextualising the trauma memory on voice-hearing and re-experiencing symptoms.

Imaginal exposure in the PE protocol involves exposure to the trauma memory for a prolonged time in sessions through repeated recounting of the trauma narrative, and listening to audio recordings of these trauma narratives between sessions. When revisiting the trauma memory, the client will typically have their eyes closed and will be asked to imagine the memory in detail in their mind, whilst recounting it in the first person, present tense. During the imaginal exposure the therapist closely monitors levels of distress using a subjective units of distress rating scale (SUDS, 0-100). Additionally, following the exposure exercise the client and therapist spend time exploring the client's reactions to the imaginal exposure, as well as any thoughts or beliefs that may be maintaining trauma-related distress. Clients were encouraged to listen to audio of the exposure session each day during the week

between sessions. The main adaptation to the PE imaginal exposure protocol for the cases described here was in the first session, which had an additional emphasis on exploring links between traumatic events and voice content.

In contrast to standard PE, in which the targeted trauma memories are those that are most intrusive, we targeted those recognised as having a link with voice content. These were identified through collaborative formulation of voice-trauma links in the baseline assessment session and session one of treatment. Following this, the trauma memories identified as the most representative of distressing voice content, or that were most intrusive were prioritised for exposure work. Initial exposure sessions focused on a whole narrative of the traumatic event. Later exposure sessions were focused on memory 'hotspots' (i.e. those parts of the memory that seemed to most represent the most distressing beliefs or emotions).

The therapy was delivered by a doctoral level, registered clinical psychologist (nine-years post-qualification) with experience in trauma-focused therapies for PTSD and in psychological therapies for psychosis (RB). Overall supervision was provided by a senior clinical psychologist with extensive experience in psychological interventions for voice-hearers (NT). In addition, consultation regarding the therapy protocol and delivery was provided by two specialists in the delivery of trauma-focused interventions for people with psychosis (SB and AH). An overview of the content of each therapy session is shown in Table 16.

Table 16. Treatment session content: Case Illustrations.

Session	Content
1	• Initial ratings of voice and trauma memory intrusion frequency and distress • Education regarding trauma and memory processing • Discussion regarding the role of avoidance • Review and elaboration of the client's trauma-voice link formulation established in the baseline assessment • An explanation of the rationale for imaginal exposure • Discussion of coping skills for managing any distress within and outside of sessions • Out of session task: client to read a hand-out regarding the nature of trauma memories and rationale for exposure
2-5	• Voice and memory intrusion ratings • Out of session task review • Imaginal exposure exercise – full narrative, or hotspot work (20-40 minutes) • Processing of cognitive and emotional aspects of the trauma • Out of session task: listen to imaginal exposure recording daily
6	• Voice and memory intrusion ratings • Out of session task review • Imaginal exposure exercise – fully elaborated trauma narratives (20 – 40 minutes) • Review of therapy progress and how client can continue to implement what they have learnt

11.5.2 Outcome measures

Tara and Laura were given outcome measures at baseline, post therapy and at one month follow up. A researcher who had not been involved in the therapy conducted all follow up assessments.

Psychiatric diagnosis was confirmed using the MINI 7.0 (Sheehan et al., 1998) and the Structured Clinical Interview for DSM 5 Borderline Personality Disorder scale (SCID 5 BPD, First et al., 1997).

Trauma history was assessed using the Life Events Checklist for DSM-5 (LEC-5, Weathers et al., 2013b) and the Childhood Trauma Questionnaire (CTQ, Bernstein & Fink, 1998).

Voice hearing severity was assessed using the Psychotic Symptom Rating Scales – Auditory Hallucinations Scale (PSYRATS-AHS; Haddock et al., 1999).

PTSD diagnosis and symptom severity was ascertained using the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Weathers et al., 2013a).

The disorganisation and intrusiveness of the trauma memory was measured using the trauma memory questionnaire (TMQ; Halligan et al., 2003). A five item disorganisation subscale assesses deficits in intentional recall and an eight item intrusiveness subscale assesses a wider range of phenomenological characteristics such as the associated emotion and reliving, vividness and 'nowness' of the memory of the event.

Posttraumatic cognitions were assessed using the Posttraumatic Cognitions Inventory (PTCI; Foa et al., 1999).

Additionally, Tara and Laura rated voice and memory intrusion frequency and distress (0-10) at the beginning of each session.

11.6 Case Descriptions

11.6.1 Tara: full remission of intrusive trauma memories and voice-hearing

Presenting problem

Tara was a woman in her late thirties who had a 23 year history of hearing derogatory and commanding voices. Tara also experienced intense mood states, stress-induced dissociation, and suicidal ideation. Tara reported hearing two main voices, identified as being the perpetrators of previous abuse she had experienced.

These voices were almost continuous and would make derogatory comments, for example "you'll never be good enough", and "you're stupid". The voices would also tell her that she should kill or harm herself.

Assessment

Tara met diagnostic criteria for borderline personality disorder and PTSD. She reported a history of emotional, physical, and sexual abuse by two prominent male figures in her life. She scored 37 on the PSYRATS-AHS, endorsing almost-continuous, threatening male voices that caused significant distress and impact on her functioning. Tara felt she had no control over the voices. She identified that the content of the voices often matched what was said to her during episodes of abuse, for example repeatedly saying, "you're stupid". Tara also heard content that she did not relate to past memories, including commands to harm herself. Tara's voices were often accompanied by intrusive images of her abusers' faces. Tara strongly endorsed items indicating that her trauma memories were intrusive and disorganised. Her scores on the PTCI suggested high levels of negative posttraumatic beliefs about herself and the world, and self-blame. Tara's pre therapy assessment scores are shown in Table 17.

Formulation

Many of Tara's voice-hearing experiences had a direct link with the content of her experiences of abuse. We therefore hypothesised that these voices were a form of posttraumatic intrusion, caused by 'unprocessed' trauma memories (stored in a sensory-perceptual, fragmented, and decontextualised form). Tara also had voice content that was not directly related to trauma content, including commands to harm herself and other derogatory comments. We hypothesised these were auditory images that had been shaped by other trauma-related sequelae, such as negative beliefs about

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herself, related low mood, and dissociative emotion regulation that had been developed as a survival strategy.

Course of therapy

The initial therapy session focused on education about the nature of trauma memories and the role of avoidance in maintaining intrusions. Tara had previously appraised her voices as being part of an 'illness', but through discussion in the sessions, identified with the idea that some of the voices might be some kind of 'replay' of trauma memories, similar to the other intrusions she was having. Tara was nervous about the idea of doing exposure work, but felt she could draw on skills she had learnt in a previous course of dialectical behaviour therapy (DBT) to help her to cope with any distress or dissociative reactions. Exposure work focused on two trauma memories that were associated with the content of Tara's voices and related intrusions. In session two, we conducted imaginal exposure to a prolonged incident of emotional and physical abuse experienced in adulthood. Session three involved exposure to one main hotspot from this memory (her abuser pinning her against a door and yelling at her). Cognitive processing work in these sessions centred on self-blaming beliefs. Tara experienced habituation of her distress response within and between exposure sessions. By session four, she reported no further intrusions relating to this particular memory and indicated that the voice of this abuser was less frequent. At this stage, Tara was still having intrusions and voices related to memories of emotional and physical abuse that occurred in childhood. Exposure sessions four and five therefore focused on a particularly intrusive memory from this time, in which her abuser called her stupid and physically assaulted her. Cognitive processing work following imaginal exposure explored Tara's belief that she was stupid, and self-blame for the childhood abuse. By session five, Tara reported minimal distress during

exposure to this memory. In session six, Tara completed a final, elaborated narrative of both memories.

Outcomes

Table 17. Tara's outcome scores

Measure (scoring range)	Baseline	Posttherapy	One month follow up
PSYRATS-AHS (0-44)	37	0	0
CAPS-5 (0-80)	55	4	0
TMQ- intrusions (0-4)	2.5	0	0
TMQ- disorganisation (0-4)	2.4	0.6	0
PTCI-total (33-231)	169	46	36
PTCI – negative self-beliefs (1-7)	5.05	1.37	1.05
PTCI- negative world beliefs (1-7)	5.14	1.71	1.14
PTCI-self-blame (1-7)	5.4	1.20	1.20

Tara's baseline, post therapy and one month follow up assessment scores are shown in Table 17, with main outcomes (PSYRATS-AHS and CAPS-5) also plotted in Figure 8. By the end of therapy and at one month follow up she was no longer hearing voices and did not meet diagnostic criteria for PTSD. Tara reported that her trauma memory was less disorganised and no longer intrusive. Her negative posttraumatic beliefs also decreased. Tara described finding the therapy challenging, but that through the process of confronting the memories, they became less vivid and distressing. Tara was also able to update unhelpful posttraumatic beliefs, stating "this was nothing to do with me, it was about [the abusers'] issues". Session-by-session ratings (see Figure 9) show an increase in posttraumatic intrusions and voices after session one and then a total remission of these experiences following session four.

Figure 8. Tara's outcome measures at pre, post and one month follow up.
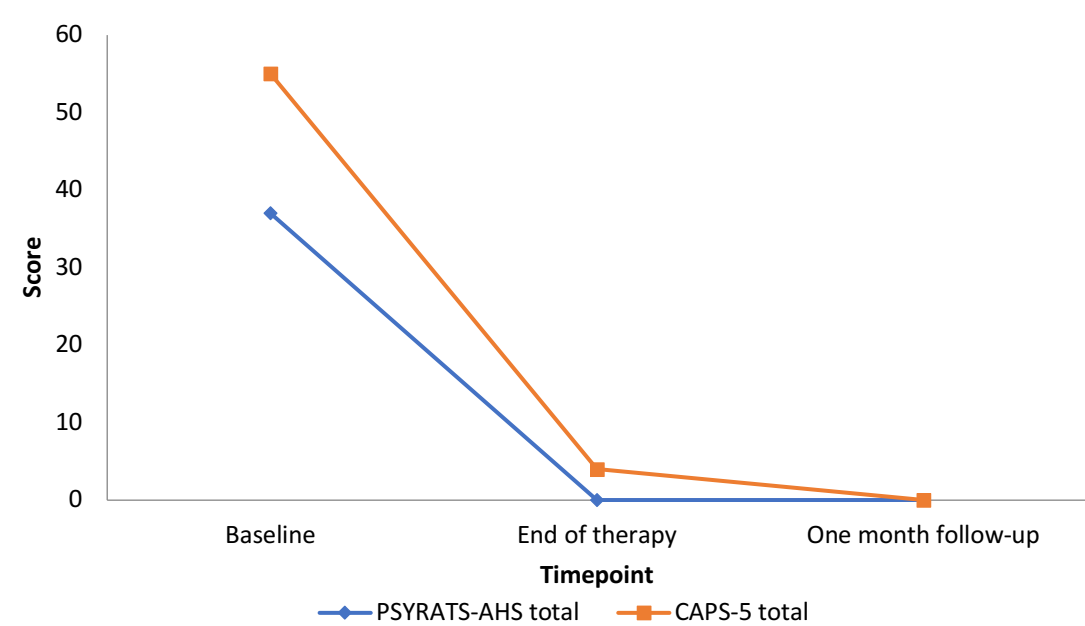
Figure 9. Tara's session-by-session ratings of voice frequency, voice distress, intrusion frequency, and intrusion distress.
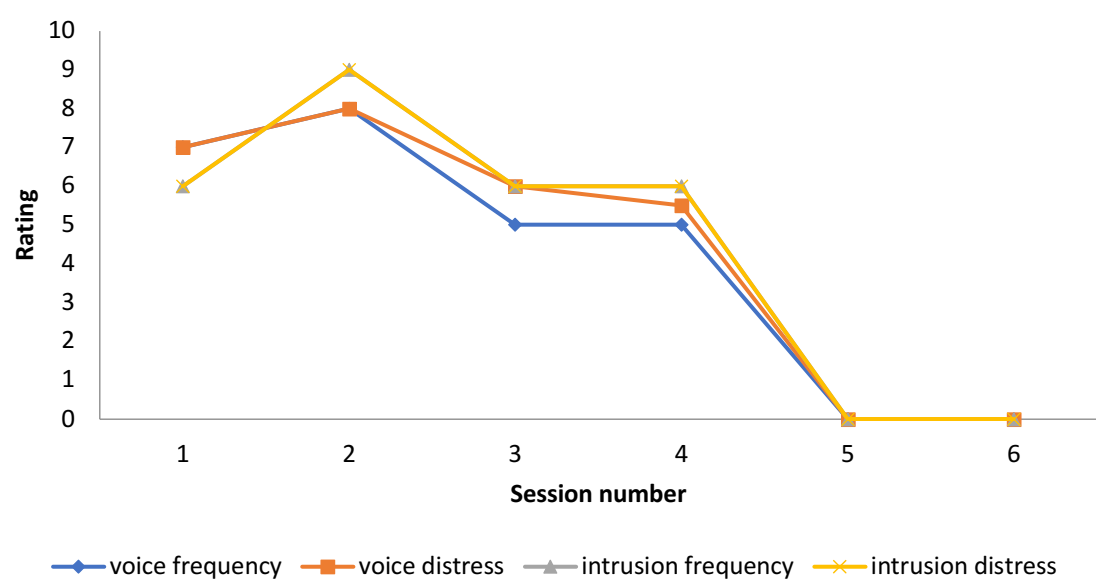
11.6.2 Symptom exacerbation and therapy termination: Laura

Presenting difficulties

Laura was a woman in her mid forties who had heard critical and bullying voices for 10 years. Laura heard multiple, unidentified voices that she perceived as coming from neighbours and passers-by. Laura described hearing people insulting and judging her, for example saying, "I don't like her". Laura was concerned that people in her local area were monitoring her and subjecting her to ongoing persecution. Laura also described persistent low mood and anxiety.

Assessment

Laura met diagnostic criteria for a major depressive disorder with psychotic features. She experienced significant emotional bullying and victimisation in her adolescent years, and throughout her adult life. This included severe bullying at school and emotional abuse by a caregiver. Laura met the symptomatic threshold for PTSD, although did not meet diagnostic criteria for PTSD based on criterion A (as her index trauma did not involve physical harm or sexual violence). Laura did not have intrusive memories of her victimisation experiences, but did experience significant emotional and physiological reactivity to reminders. Laura scored 34 on the PSYRATS-AHS, endorsing almost continuous, derogatory voices, causing significant distress. Laura felt she had no control over the voices. Laura did not identify that any of the content of the voices was a direct 'replay' of things heard during her trauma. Laura's TMQ scores suggested that her trauma memories were not disorganised but were intrusive. Her scores on the PTCI suggested high levels of negative posttraumatic beliefs about herself and the world, and self-blame. Laura had previously had cognitive behavioural therapy for her voices, with a particular focus on coping strategy enhancement.

Formulation

We identified that Laura's voices had a thematic link to her past victimisation experiences. During these experiences, she felt vulnerable and humiliated and this was mirrored in the content of the voices. We hypothesised that Laura's negative beliefs about herself and others were contributing to the content of the voices. Laura's voices were also serving as a reminder of her victimisation experiences and triggering trauma-related emotional and physiological responses. Laura was then enlisting a learnt survival strategy of hypervigilance to manage these difficult feelings, which was leaving her more vulnerable to noticing the comments from her neighbours.

Course of therapy

Laura attended two therapy sessions. The first session focused on education about the nature of trauma memories, the role of avoidance, and exploring the links between Laura's voices and other posttraumatic sequelae. Laura understood the rationale for exposure work and was keen to reduce the impact of her negative posttraumatic beliefs and reduce her reactivity to reminders of the victimisation. The first exposure session focussed on a memory of bullying from high school in which she was publicly humiliated by a group of girls. Laura reported high levels of distress, but did experience habituation within the session. Cognitive processing work after the exposure exercise focused on reappraising negative peri and posttraumatic beliefs about herself. Several days after this session Laura phoned the therapist and stated that she did not want to continue with the therapy. After the session she experienced high levels of distress, and this was exacerbated when she listened to the session audio at home. She also reported an increase in the voices and victimisation by her neighbours, which made it too difficult to confront and process her past victimisation experiences.

Outcomes

Table 18. Laura's outcome scores

Measure (scoring range)	Baseline	Posttherapy	One month follow up
PSYRATS-AHS (0-44)	34	39	35
CAPS-5 (0-80)	25	36	18
TMQ- intrusions (0-4)	3.5	3	1.5
TMQ- disorganisation (0-4)	0.6	1.8	3
PTCI-total (33-231)	160	166	177
PTCI – negative self-beliefs (1-7)	4.68	4.79	5.16
PTCI- negative world beliefs (1-7)	5.43	6.00	6.43
PTCI-self-blame (1-7)	4.20	4.40	4.80

Laura's baseline, posttherapy and one month follow up assessment scores are shown in Table 18, with main outcomes (PSYRATS-AHS and CAPS-5) in Figure 10. Laura experienced an increase in voices and PTSD symptoms post therapy, but this had decreased again by one month follow up. Laura's session-by-session ratings (see Figure 11) also show that her voices and memory intrusions worsened after the first exposure session, prior to her ceasing the therapy. The process measures suggest that the intrusiveness of Laura's trauma memories did decrease, but that the disorganisation of this memory and her negative posttraumatic beliefs actually increased.

Figure 10. Laura's outcome measures at baseline, end of therapy and one month follow up.
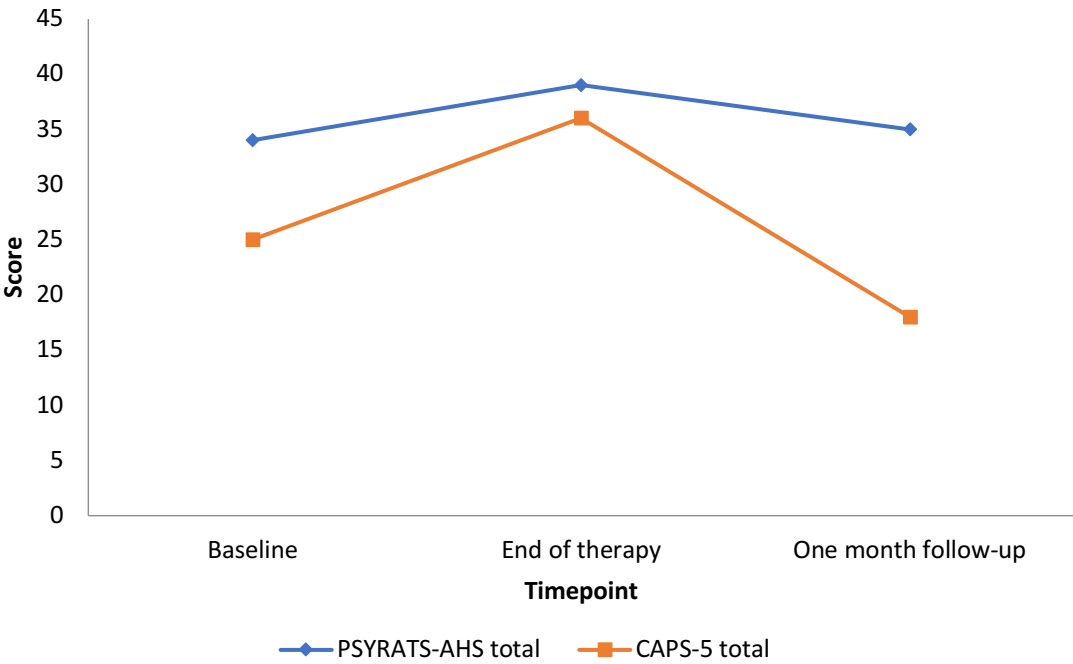
Figure 11. Laura's session-by-session ratings of voice frequency, voice distress, intrusion frequency, and intrusion distress.
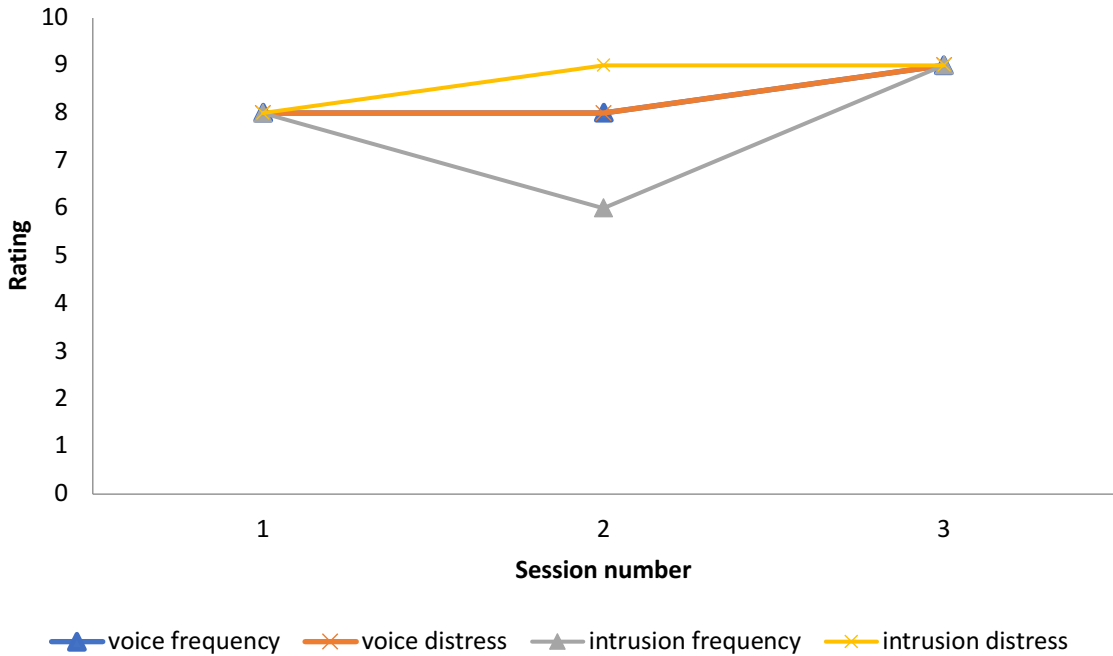
Note: Laura gave her session 3 ratings over the phone one week after session 2.

11.7 Discussion

Tara and Laura's therapy outcomes are at the extreme ends of our experience in delivering imaginal exposure for trauma-related voices. Examining the characteristics and experiences of 'extreme responders' to a therapy can help to inform therapy dissemination and development (e.g. Coffman, Martell, Dimidjian, Gallop, & Hollon, 2007). We use Laura and Tara's experiences to illustrate learning that is also reflective of our wider experience of delivering imaginal exposure for trauma-related voices.

11.7.1 Symptom exacerbation and the tolerability of exposure-based trauma-focused therapies for trauma-related voices.

There have long been concerns that trauma-focused therapies may lead to symptom exacerbation for people with psychosis, however recent trials have indicated this is not the case, at least in controlled trial scenarios, (see Brand et al., 2017 for a review). A qualitative study in an early psychosis population, on the other hand, included some reports of symptom exacerbation following talking about trauma (Tong et al., 2017). Symptom exacerbation was relatively transient and did not affect outcomes (Tong et al., 2017). This is line with literature relating to the use of trauma-focused therapies for PTSD, which has indicated that many people do experience symptom exacerbation; but that this group go on to have clinically significant improvement by the end of therapy (Larsen, Wiltsey Stirman, Smith, & Resick, 2016).

Our experience has been that temporary symptom exacerbation is a common experience in the early sessions of exposure therapy for trauma-related voices. Both Laura and Tara experienced increases in posttraumatic intrusions and voices in their early sessions, however Tara went on to experience significant reduction in these symptoms and Laura's scores returned to baseline levels at one month follow up. In

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line with previous research, this suggests a transient increase in symptoms that does not affect outcomes. Our experience has also been that most people find this temporary symptom exacerbation tolerable, but that some find it unmanageable and may discontinue therapy as a result.

We suggest that it is important to consider the possibility of symptom exacerbation when planning trauma memory exposure work. Clients should be informed that temporary distress and symptom exacerbation might be a possibility and necessary supports for managing this put in place. Several factors may impact on an individual's ability to tolerate temporary symptom exacerbation. In Tara's case, her living context, prior therapy experience, and appraisals of her voices contributed to her positive experience with therapy. Tara was living in a safe environment and no longer felt under threat from other people. She had completed a course of DBT 10 months prior and this gave her confidence that she could manage the therapy. She also had an internal appraisal of her voices (seeing them as part of her diagnosis, or as trauma memories), which likely reduced her reactivity to increases in voices. Laura, on the other hand, did not feel safe in her home environment due to her concerns about ongoing victimisation. Her appraisal that the voices were coming from her neighbours, meant that the increase in voices in the first two sessions was very difficult to tolerate. This did not appear to be mitigated by the fact she had previously had cognitive behavioural therapy for voices, including coping strategy enhancement. When treating PTSD, current safety is a priority and trauma-focused work would ideally not commence until a person is in a sufficiently stable and safe environment. This may also be a key consideration in working with people with trauma-related voices. Persecutory appraisals of the voices mean that clients may not have a subjective sense of safety from which to process past traumas. Laura's feedback was

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that her current lack of safety meant that she did not feel able to manage processing her memories of past victimisation. In this situation, it may be that work needs to be done with persecutory beliefs and associated distressing appraisals of voices (e.g. using CBTp) prior to any memory exposure.

Given the possibility of transient symptom exacerbation, we would suggest that the timing of delivering exposure-based trauma-focused therapy is most appropriately negotiated within a safe therapeutic relationship. Clients and clinicians can collaboratively weigh the risks of temporary symptom exacerbation against the potential benefits of exposure work, and (if necessary) build internal and external contexts that make this more tolerable if a client wishes to proceed. This work would be akin to phase one in a phase-based approach to trauma therapy, in which the focus is on safety and stabilisation (Herman, 1992) and might involve practical support to ensure a safe living situation, strengthening of coping skills, and therapies that can reduce threat based appraisals and emotions (e.g. CBTp, including third wave approaches such as compassion focused therapy). Additionally, this needs to be monitored and revisited throughout the therapy process. Importantly, not everyone appears to need this preparation work and, given the potential benefits, we believe that it is important that exposure-based trauma therapies are not unnecessarily delayed when collaborative formulation indicates the relevance of decontextualised trauma memories.

11.7.2 Who is most likely to benefit from exposure-based trauma-focused therapies for distressing voices?

It is not yet clear how to determine who will benefit most from trauma-focused therapies for voice-hearing experiences. Trauma-voice links are often complex and heterogeneous, and trauma memories are only relevant for a proportion

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of people (Hardy, 2017). Based on clinical experience (including the clients presented here) we hypothesise that imaginal exposure to the trauma memory is most appropriate when voice-hearing experiences are directly related to trauma memories, particularly when aspects of voice content represent a re-experiencing of trauma content. The presence of related intrusive trauma memories may also suggest that imaginal exposure to the trauma memory is indicated. In Tara's case, many (but not all) of her voices had a direct link with her traumatic experiences (i.e. were exact replays of content heard at the time of the traumas). She also had other, related, intrusions to the trauma memory (images of her abuser's faces). Our formulation of Tara's voices was that they were related to trauma memory encoding that was predominantly at a perceptual level, such that encoded sensory based, decontextualised memories were being re-experienced as voices and other related intrusions. It appears that the exposure therapy worked through the mechanisms we might expect – elaborating the trauma memory into a more contextualised, episodic form, and thus reducing intrusive re-experiencing.

Conversely, Laura's voices had a thematic link with her traumas (rather than being direct replays) and she did not have any related intrusive memories of her victimisation experiences. The voices were formulated to be auditory images arising as a result of negative beliefs about herself and others, as well as hypervigilance to social threat (learnt as a survival mechanism). Given the hypothesised mechanisms involved in Laura's voices, trauma-focused therapies primarily targeting negative peri or posttraumatic beliefs (for example cognitive therapy or imagery rescripting) and therapies that help to down regulate threat-based attentional systems through strengthening safety and soothing systems (for example, compassion focussed therapy or DBT) may have been more tolerable and effective. The fact that Laura did not have

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intrusive memories of her victimisation experiences may also be important in understanding why imaginal exposure was less tolerable and effective, since imaginal exposure has a much clearer rationale (and demonstrated effectiveness) in the presence of intrusive trauma memories.

11.7.3 Research Implications

The hypotheses discussed here will need to be explored further in both qualitative and quantitative studies, testing a range of trauma-focused approaches for people with trauma-related voices. The diversity in treatment response described here suggests that future trials should aim to measure the full range of outcomes, rather than focusing on group means, which can obscure between-person differences in treatment response. Particularly, studies can focus on reporting the number of people experiencing reliable change in both a positive and a negative direction (to capture those who significantly improve or deteriorate). Additionally, well-powered trials are needed in order to understand individual factors that moderate response to different trauma-focused therapies. This will provide a more robust evidence base for clinical decision making about safe and effective timing and delivery of trauma-focused therapies for distressing voices. Finally, trials are needed that compare the acceptability, safety, and efficacy of phase-based trauma therapies (i.e. those that include other 'stabilising' therapies prior to trauma-focused work) with standard trauma-focused therapies.

11.8 Conclusion

Tara and Laura's stories illustrate the potential therapeutic importance of understanding associations between trauma and voices, with those with a direct link perhaps more likely to see benefits from exposure therapy, while those with indirect links may benefit more from trauma-focused and non-trauma-focused approaches that

target beliefs and emotion regulation. Additionally, we have highlighted the potential that exposure therapy may be less tolerable when clients have persecutory appraisals of their voice-hearing experience, given the ongoing sense of physical or social threat. Finally, our experience of delivering short-term therapy in which exposure is commenced in session two has shown that some people find this manageable, while others may benefit from a focus on creating objective and subjective safety prior to exposure work. These hypotheses borne from our clinical experience will need further exploration in qualitative and quantitative treatment research using a range of trauma-focused approaches for people with trauma-related voices.

PART III: GENERAL DISCUSSION

Chapter Twelve: Discussion

The overall aim of this thesis was to explore the role of PTSD symptoms and trauma memory processing as putative psychological mechanisms involved in auditory hallucinations, and as a potential target for treatment using trauma-focused psychological therapies. The three empirical studies presented in the preceding chapters were designed to address this aim. This chapter provides a synthesis of the findings from these empirical studies in relation to this overarching aim. Reflection on the findings provides integration of the individual studies into a unified body of work. The data presented are then considered in the context of the literature reviewed in Part I of the thesis. Further, a critical review of study methods is provided. Finally, implications for future clinical practice and research are explored.

12.1 Summary of Findings in Relation to Thesis Aims

12.1.1. The role of PTSD symptoms and trauma memory processing as potential psychological mechanisms involved in auditory hallucinations.

Firstly, the empirical studies aimed to extend upon previous research implicating posttraumatic stress symptoms and the nature of trauma memory processing in auditory hallucinations. As outlined in the published opinion piece presented in Chapter Six, the majority of evidence in this area prior to this thesis had been cross-sectional, and therefore limited in establishing the association of aggregated, retrospective measures of PTSD symptoms and auditory hallucinations. The opinion piece outlined two methodological paradigms that might extend the evidence beyond association: the use of ecological momentary assessment and the use of interventionist–causal models. The three empirical studies were grounded in these approaches.

Study One used an EMA methodology to examine moment-to-moment associations between trauma memory intrusions, hyperarousal, and avoidance. Using this micro-longitudinal approach, Study One found that proximal (occurring in the hour preceding the EMA signal) trauma memory intrusions were significantly associated with auditory hallucinations. An increase of one point on the trauma memory intrusions scale within the hour prior to the signal was associated with a 43% increased likelihood of an auditory hallucination at the signal when proximal avoidance, hyperarousal, and auditory hallucinations at the previous time point were controlled. This suggests a role for trauma memory intrusions in auditory hallucinations above and beyond that of hyperarousal and avoidance. Indeed, proximal avoidance and hyperarousal were not significantly associated with auditory hallucinations. Lagged (occurring in the previous time period) trauma memory intrusions, avoidance, and hyperarousal were not significant predictors of auditory hallucinations. This suggests that any relationship between trauma memory intrusions and auditory hallucinations is present within a relatively short timeframe, rather than over an extended period. Finally, the EMA study provided an initial indication of a significant moderated relationship; the relationship between both proximal and lagged trauma memory intrusions and auditory hallucinations was moderated by the nature of the link between auditory hallucination content and the index traumatic event. Specifically, those with a direct link between the content of their auditory hallucinations and the index traumatic event had a stronger relationship between trauma memory intrusions and auditory hallucinations.

Overall, these findings provide an advance in understanding the role of PTSD symptoms in trauma-related auditory hallucinations by providing preliminary data regarding how these symptoms interact on a moment-to-moment basis in daily life.

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Results suggest an important proximal association between auditory hallucinations and trauma memory intrusions that may be stronger and more enduring for a small group who have direct content links between their auditory hallucinations and past trauma.

With regard to exploring the role of trauma memory processing in auditory hallucinations, Study One did not find that trauma memory processing (as measured by the trauma memory questionnaire) was a moderator of the relationship between trauma memory intrusions and auditory hallucinations, as might have been expected if trauma memory processing was an underlying factor involved in this relationship.

The findings from Study One need to be considered in light of important methodological limitations that will be discussed further in section 12.4. While Study One does represent an advance in knowledge regarding the role of PTSD symptoms, the findings are still that of an association. Indeed, the fact that there was only a significant main effect found for the proximal relationship, but not the lagged relationship means that it is difficult to draw any definitive conclusions regarding the temporal ordering of the experiences. Additionally, without controlled manipulation of the variables of interest, it is not possible to infer that their role is causal.

As highlighted in the opinion piece in Chapter Six, the most robust exploration of the role of PTSD symptoms and trauma memory processing in auditory hallucinations may be achieved using controlled trials of interventions that reduce PTSD symptoms and process trauma memories, in an interventionist–causal approach. Study Two and Study Three therefore provide initial data to address this aspect of the thesis aim by paving the way for a trial using an interventionist–causal approach. The meta-analysis (Study Two) indicated that evidence-based trauma-focused treatments for comorbid PTSD in psychotic symptoms may have secondary

effects on reducing positive symptoms of psychosis; however, these effects were not maintained at follow up. Of note, the meta-analysis also suggested that the included studies only achieved small effects on PTSD symptoms at post treatment that were not significant at the follow up timepoint. The fact that the impact on PTSD symptoms was not established as clearly as might be expected limits conclusions within an interventionist–causal framework (since the intervention needs to act on the putative causal variables of interest to ascertain their impact on the dependent variable of interest). The meta-analysis established that treatments including exposure to the trauma memory had significantly larger effects on PTSD symptoms, suggesting that these treatments are well placed to be used in an interventionist–causal approach in the future. Overall, the findings from the meta-analysis suggest that reductions in PTSD symptoms may be related to reductions in positive symptoms of psychosis, thus supporting their potential causal role. The meta-analysis was not able to provide conclusive data regarding auditory hallucinations specifically (since only two studies measured this as a separate outcome). Additionally, the interventions included in the meta-analysis predominantly targeted trauma memories related to PTSD symptoms, rather than trauma memories related to auditory hallucinations. Thus it was concluded that a robust assessment of the role of PTSD symptoms and trauma memory processing in auditory hallucinations requires an intervention that targets the index memories that are of potential causal relevance to the auditory hallucinations.

Study Three, the pilot study of imaginal exposure for trauma-related auditory hallucinations, also provides preliminary data regarding the putative role of PTSD symptoms and trauma memory processing in auditory hallucinations. The intervention reduced PTSD symptoms as well as the intrusiveness and sensory-perceptual quality of the trauma memory. In addition, there were large estimated effects on the overall

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severity of auditory hallucinations. Taking an interventionist–causal approach, these tentative findings are in keeping with a causal role of PTSD symptoms and trauma memory processing in auditory hallucinations. The large variance in individual response to the intervention implies that PTSD symptoms and trauma memory processing may be of causal relevance for a subgroup of individuals. These conclusions are based on estimated, uncontrolled effects from a small number of participants and are therefore limited in informing an interventionist–causal assessment of the role of PTSD symptoms and trauma memory intrusions in auditory hallucinations. Nevertheless, these findings do indicate a larger study that is adequately powered and well controlled may be warranted to provide more definitive answers regarding the causal role of PTSD symptoms and trauma memory processing in auditory hallucinations using an interventionist–causal approach.

12.1.2 PTSD symptoms and trauma memory processing as a potential target for treatment.

The second aspect of the thesis aim was to examine the potential of interventions that target PTSD symptoms and trauma memory processing for treating auditory hallucinations. Using EMA, Study One provided preliminary evidence regarding the potential of targeting PTSD symptoms as a treatment for auditory hallucinations. The finding that trauma memory intrusions have momentary associations with auditory hallucinations supports the assertion that treating trauma memory intrusions may have an impact on auditory hallucinations.

Study Two and Study Three have provided data specifically relating to the potential for PTSD symptoms and trauma-memory processing as targets for treatment, namely; Study Two and Study Three provide initial indications of the feasibility of trauma-focused therapies for auditory hallucinations, how acceptable these

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interventions may be, and of their potential effects on auditory hallucinations. Results relating to feasibility, acceptability and potential effects are outlined separately below.

Study Three addressed the feasibility of treating trauma-related auditory hallucinations with exposure-based trauma focused therapies that target PTSD symptoms and trauma memory processing. There were some feasibility issues in using brief, standard protocol exposure-based trauma-focused therapies to treat auditory hallucinations. There were low referral rates and low uptake among those who showed initial interest and were screened over the telephone. When people were told about the imaginal exposure intervention, 43% declined participation on the basis of not wanting to undertake this specific therapy. Not only does this have implications for the feasibility of a future randomised-controlled trial (discussed in more detail in section 12.6), but it also has implications for feasibility of implementing this intervention in clinical practice. Even if an intervention is effective, it is of little value if it is not taken up by the people who may benefit. The clinical implications of this feasibility issue will be discussed further in section 12.5.

Study Three also provided evidence regarding the acceptability of trauma-focused therapies that target PTSD symptoms and trauma memory processing for treating trauma-related auditory hallucinations. Data from all of the participants who completed the satisfaction survey (*n*=12) suggested that people were generally satisfied with the quality, amount, content, and effects of the imaginal exposure intervention. This suggests that this approach is acceptable for many people (particularly those who complete the full intervention). In contrast, this same group did also report significant distress in sessions, with 25% reporting this to be unmanageable. Three participants who discontinued the intervention reported increases in distress and both psychotic and PTSD symptoms (though one participant

did not relate this to the study intervention). This suggests that symptom exacerbation and distress are commonly experienced in the early sessions of the intervention and that this is not tolerable or acceptable for a minority of people and may contribute to discontinuation of the therapy in this group. This is important information for developing the intervention for use in clinical practice, and as an object of enquiry in further clinical trials. Addressing these acceptability issues in clinical practice and future research will be discussed in sections 12.5 and 12.6 respectively.

       Study Two and Study Three provide preliminary data regarding the effects of trauma-focused therapies that target PTSD symptoms and trauma memory processing for treating trauma-related auditory hallucinations. The meta-analysis in Study Two found small, but significant secondary effects of trauma-focused therapies on positive symptoms of psychosis at post treatment, but this effect was not maintained at follow up. This is promising, but the loss of effect at follow up means that any gains made over and above treatment as usual do not appear to endure beyond the end of therapy. This suggests that the benefit of treating trauma memories may only be short lived, or alternatively, that the effect seen on psychotic symptoms was an artefact of general therapy effects (e.g. contact with a therapist) that did not endure beyond the therapy itself. The meta-analysis did not provide robust information regarding the effects of trauma-focused therapies on auditory hallucinations specifically; only two studies were included in this analysis, yielding minimal and nonsignificant effects. Notably, one of the included studies in this analysis did not include an exposure-based trauma-focused therapy (Steel et al., 2017) and therapies that did not include exposure to the trauma memory were found to have significantly smaller effects on PTSD symptoms than those that did. To fully assess the effect of trauma-focused therapies that address PTSD symptom and trauma memory processing, it was deemed important to

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specifically assess the effect of potentially more 'potent' exposure-based therapies. In addition, the assessment of the effects of trauma-focused therapies on auditory hallucinations in the meta-analysis was limited by the fact that auditory hallucinations were not targeted as the primary outcome, thus memories focused on in therapy were not necessarily those that were linked to the auditory hallucinations.

Study Three built upon the findings from the meta-analysis and examined the potential effects of an exposure-based trauma-focused therapy specifically targeting trauma-related auditory hallucinations. This study found large estimated effects on auditory hallucination severity one month following the intervention; however individual participant response to the intervention was highly variable, meaning that confidence intervals around the estimate were wide. This suggests that imaginal exposure may be an effective intervention for auditory hallucinations, but that there could be important factors that moderate individual treatment response. The intervention had large estimated effects on PTSD symptoms and on the intrusiveness of the trauma memory and sensory-perceptual detail in the trauma narrative, indicating that the intervention did successfully target some putative mechanisms of interest. Conversely, reductions in the disorganisation of the trauma memory and increases in cognitive processing in the trauma narrative were minimal, suggesting that some aspects of trauma memory processing were not effectively targeted. Also, there were medium estimated effects on negative posttraumatic beliefs, suggesting that this may also be a mechanism of change. All of these findings from the pilot trial need to be considered in light of methodological limitations that will be discussed further in section 12.4.

12.2 Synthesis of Findings Between Studies

The three studies utilised different methodologies to address the role of PTSD symptoms and trauma memory processing in auditory hallucinations, and as potential targets for treatment. Considering the correspondence of findings across these studies links them together as a cohesive body of work and allows for greater confidence in the conclusions that can be drawn.

Firstly, a number of findings across the studies implicate trauma memory intrusions as having particularly important associations with auditory hallucinations. The EMA data found that trauma memory intrusions showed momentary associations with auditory hallucinations, but there was not a relationship with hyperarousal and avoidance symptoms. This is in alignment with the pilot treatment study that found imaginal exposure had large estimated effects on auditory hallucinations and highlighted the intrusiveness of the trauma memory as a potentially important process of change during the intervention.

Secondly, a finding that is corroborated across Study One and Study Three relates to the content link between the trauma memory and the auditory hallucination. Study One found that the small group of people with a direct content link between their auditory hallucination and the index trauma had a stronger and more enduring association between moment-to-moment trauma memory intrusions and auditory hallucinations. Similarly, visual inspection of mean session-by-session data in Study Three suggested that the small group who had direct content links between their trauma memory and their auditory hallucination responded more dramatically to the intervention. While preliminary, and based on small numbers, these findings suggest there is a small group of people for whom trauma memory intrusions may be of importance, and for whom exposure-based trauma-focused therapies may be most

potent and that this group may be characterised by direct content links between their auditory hallucinations and the traumatic event.

12.3 Thesis Findings in the Context of Previous Theory and Research

The findings of the three empirical studies can be situated within, and inform, several areas of previous theory and research. The results may be of relevance to neurocognitive and cognitive behavioural theories that have attempted to explain the causal processes involved in auditory hallucinations. Of particular interest is how the findings fit with trauma-informed models of auditory hallucinations that have explicitly drawn upon psychological theories of PTSD to understand how traumatic events may lead to auditory hallucinations. Additionally, it is informative to consider the data in the context of a small body of research examining trauma-focused therapies for auditory hallucinations, a larger body of research that has considered the general feasibility and acceptability of exposure-based trauma-focused therapies, and a handful of psychological treatment studies that have reported instances of full remission of auditory hallucinations. Each of these areas will be explored separately below.

12.3.1 Neurocognitive models of auditory hallucinations

Neurocognitive models have been influential in understanding the underlying processes that may be involved in auditory hallucinations, but have not been widely translated into psychological therapies. The findings of this study are of most relevance to Waters et al.'s (2006) model, which suggests that auditory hallucinations are caused by unintentional activation of memories and other mental representations. In this model, a combination of impairments in intentional inhibition and contextual memory are postulated to contribute to the occurrence of auditory hallucinations. Difficulties in inhibiting mental events leads to intrusions of memory representations

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and disturbances in contextual binding mean that these memories are not identified to be internally generated and are experienced as external. The findings of this thesis are consistent with this model, suggesting that some auditory hallucinations may be shaped by trauma memory intrusions, and that trauma memory processing may be implicated in this. Waters et al. do not specifically implicate traumatic memories in their theory, but instead theorise that any spurious memory material can form the basis of auditory hallucinations. The findings of this thesis suggest that trauma memory intrusions may play a particular role, and therapies that specifically contextualise trauma memories may impact upon auditory hallucinations (again suggestive of a specific role of trauma memories and trauma memory processing); however, it is also possible that the impact of trauma memories and trauma memory processing is not only a trauma-related process, but is a specific example of a more general role of difficulties with the inhibition and contextualisation of memories.

12.3.2 Cognitive behavioural models of psychosis

Morrison (2001; Morrison, Haddock, & Tarrier, 1995) theorised that intrusive thoughts images and impulses form the basis of psychotic experiences. The findings of the three studies in this thesis provide support for the notion that intrusions (particularly memory intrusions) into awareness may be intricately associated with auditory hallucinations. In contrast, Morrison did not explore the role that trauma and adversity may play in the genesis of intrusions. Instead, trauma and adversity were considered to play a role in psychotic experiences primarily at the level of beliefs and attributions; traumatic and adverse experiences were hypothesised to lead to faulty self and social knowledge (e.g. 'other people are dangerous') that increases the likelihood of external, threatening interpretations of anomalous experiences. The findings of the present research indicate that trauma and adversity may also play a

role at the level of generating intrusions – specifically that decontextualised trauma memories may form the basis of some intrusions. Study Three did also find that imaginal exposure had large effects on posttraumatic beliefs, providing preliminary indication that changes in auditory hallucinations may also have been associated with changes at the level of posttraumatic beliefs, thus supporting Morrison's theory (Morrison, 2001). However, it is also of note that the meta-analysis (Study One) indicated therapies that focused primarily on addressing posttraumatic beliefs, and did not involve trauma memory processing, had smaller effects, which is suggestive of a more notable role for trauma memory processing than for posttraumatic beliefs.

Garety et al.'s (2001) cognitive behavioural model of positive psychotic symptoms has also emphasised the importance of trauma and adversity; primarily in shaping appraisals and beliefs about anomalous experiences (which are argued to be the basis of psychotic symptoms). Garety's model also briefly outlines the role of memories of difficult life experiences in causing anomalous experiences. Drawing on the early theories of Hemsley (1994), Garety et al. (2001) outlined that triggering events (stressful or adverse experiences) might cause a weakening in the influence of stored memories (contextualisation) on information processing, leading to unstructured and ambiguous sensory input and the subsequent intrusion into consciousness of unintended material from memory. This implication of traumatic and adverse events at the level of causing memory intrusions is consistent with the findings of this thesis.

Cognitive behavioural models of psychosis have also placed the role of arousal and avoidance centrally in their conceptualisation of the genesis and maintenance of psychotic experiences. Garety et al. (2001) suggest that emotional disturbance (such as high levels of arousal) influence the content and appraisal of

anomalous experiences and that this leads to these experiences becoming 'psychotic'. Similarly, Morrison (2001) highlights high levels of arousal as a maintaining factor in psychotic experiences. The findings from Study Two did not indicate that hyperarousal had a momentary association with auditory hallucinations, which does not provide support for these theories. Study Two focused on measuring the impact of state fluctuations in hyperarousal so it is possible that trait hyperarousal has more influence than momentary fluctuations in hyperarousal.

Morrison et al. (1995) suggested that avoidance of intrusions plays a central role in auditory hallucinations, hypothesising that auditory hallucinations are intrusions that are incompatible with a person's beliefs and are therefore disavowed (and identified to be from an external source). This avoidance of intrusive material was also highlighted as a maintaining factor in Morrison's later model of psychosis (Morrison, 2001) and in Garety et al.'s model (2001). Posttraumatic avoidance was not found to have a significant main effect on auditory hallucinations in Study Two; however, a stronger relationship between avoidance and auditory hallucinations was found specifically for the group who met diagnostic criteria for PTSD. Reducing posttraumatic avoidance is a key aspect of imaginal exposure and has been suggested to be a key mechanism of change (Foa & Rothbaum, 1998). Thus, the fact that imaginal exposure did have large (albeit variable) effect on auditory hallucinations may also provide some support for a role of avoidance.

The discrepancies between the findings of this thesis and dominant psychological models of psychosis are of potential importance for informing therapy development. The central focus on beliefs and attributions in these models has led to psychological therapies predominantly focusing on change at the level of beliefs and attributions (for example, Birchwood et al., 2014). The finding that intrusions

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themselves may be amenable to psychological therapy (i.e. through contextualising and processing the memories or images that may be giving rise to intrusions) indicates that this shift in focus may be a fruitful direction for treatment development. This is also in line with the priorities of many people who seek psychological therapy for distressing auditory hallucinations – to reduce the frequency of the experience, rather than just focusing on changing their interpretations of this experience.

12.3.3 Psychological theories of auditory hallucinations that have been informed by theories of PTSD

The aims of this thesis were primarily based upon a body of literature that has used theory and research from the area of PTSD to inform understanding of the role that traumatic events may play in auditory hallucinations. Morrison, Frame, and Larkin (2003) proposed that PTSD and psychosis may represent a spectrum of posttraumatic reactions, with similar psychological mechanisms involved. Morrison identifies that intrusions that form the basis of psychotic symptoms could themselves be trauma-related, or that beliefs about self and world that develop as a result of traumatic events may influence interpretations of intrusions (as external threats). As discussed in section 12.3.2, this thesis was mainly concerned with the former suggestion – that trauma memories may be the intrusions that form the basis of some auditory hallucinations. The findings are in keeping with this suggestion. Specifically, all three studies do indicate that intrusive trauma memories may be associated with some auditory hallucinations. These findings also support Steel et al. (2005) and Hardy's (2017) models, which implicate trauma memory intrusions centrally in understanding auditory hallucinations. The momentary association between trauma memory intrusions and auditory hallucinations found in Study One is in keeping with previous cross-sectional research that has identified that trauma memory intrusions

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are associated with auditory hallucinations in trauma affected populations (Alsawy et al., 2015; Gracie et al., 2007) and that trauma memory intrusions may mediate the relationship between traumatic events and auditory hallucinations (Peach et al., 2018). This study extends upon these findings by further explicating the momentary relationship between these experiences. Indeed, the fact that there was a significant main momentary effect of proximal trauma memory intrusions, but not of more distal trauma memory intrusions provides further information about temporal relationships; if auditory hallucinations are a type of trauma memory intrusion then we would expect these experiences to have immediate associations, rather than trauma memory intrusions being a predictor of auditor hallucinations over a longer time period.

Steel et al. (2005) and Hardy's (2017) models go beyond just conceptualising auditory hallucinations as trauma memory intrusions and provide theory relating to the psychological mechanisms through which trauma memories might become intrusive and no longer be experienced as memories, but as auditory hallucinations. Both theories highlight the importance of the information processing during traumatic events, in which encoding is predominantly 'data-driven' (leading to memories that are predominantly sensory-perceptual and fragmented in terms of relation to place and time) and pre-existing difficulties with contextual processing in leading to intrusions that lack autonoetic awareness and thus are experienced as a current external threat. The findings from the empirical studies undertaken provide some support for this premise. Study Three showed that imaginal exposure did have an impact on some relevant aspects of trauma memory processing. The level of sensory-perceptual detail in the trauma narrative showed large decreases between the first and final exposure session, and the self-rated intrusiveness of the trauma memory also showed large reductions between baseline and one month follow up. It was not possible to formally

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assess these variables as mediators of change in the context of a small pilot trial; however, these findings provide tentative evidence that these changes in the nature of the trauma memory may be processes of change in imaginal exposure for trauma-related auditory hallucinations. In contrast, the disorganisation of the trauma memory and the level of cognitive processing in trauma narratives showed little change following imaginal exposure, suggesting that these aspects of the trauma memory were not associated with any change seen in auditory hallucinations. These findings provide preliminary and partial support for the importance of trauma memory processing in auditory hallucinations, and support previous research that has implicated these processes (Geddes et al., 2016; Marks et al., 2012; Steel et al., 2008). On the other hand, Study One did not find that trauma memory processing was a moderator of the momentary association between trauma memory intrusions and auditory hallucinations, which does not support the assertion that the nature of trauma memory processing is of importance in the relationship between trauma memory intrusions and auditory hallucinations. There are some fundamental difficulties in the measurement and reporting of trauma memory intrusions and trauma memory processing that are notable in interpreting the findings of these studies. Firstly, measuring the nature of trauma memory processing post trauma has been based on a variety of measures that are not well validated and has generally provided heterogenous results (Crespo & Fernandez-Lansac, 2016). The Trauma Memory Questionnaire (used to measure the nature of the trauma memory in Study One and Study Three) includes some items that may be reflective of decontextualisation (e.g. items capturing 'nowness' and sense of reliving) and others that may tap constructs that are related to data-driven processing (e.g. items capturing vividness). This makes it difficult to interpret the findings using this measure. Secondly, the fact that these

theories suggest that auditory hallucinations are a type of trauma memory intrusion that occurs without autonoetic awareness presents a methodological challenge. If auditory hallucinations are trauma memories that are so decontextualised that they are not recognised as memories, then we would perhaps not expect people to recognise or report the presence of trauma memory intrusions. Selection of the sample for Studies One and Three required that participants had made some links between their trauma experiences and their auditory hallucinations. This was necessary for delivery of the therapy and measurement of posttraumatic stress symptoms (which both required rapid identification of a relevant index trauma memory), however may have had implications for testing the theory that some auditory hallucinations are decontextualised trauma memory intrusions. The fact that the sample recognised that trauma memories might be involved in their auditory hallucinations may mean they were not representative of the group proposed to have decontextualised trauma memories, thus limiting conclusions about the importance of decontextualisation.

Hardy's model (2017) is perhaps the most elaborated model of the involvement of posttraumatic processes in psychotic symptoms, incorporating evidence relating to memory processes, emotion regulation, and schematic beliefs into two proposed pathways from trauma to psychotic experiences. Hardy considers the development and maintenance of auditory hallucinations in the first pathway to be primarily linked to the encoding and retrieval of episodic memories, with emotion regulation and beliefs also playing a secondary role in this pathway. The content of auditory hallucinations in this first pathway is likely to represent direct 'reliving' of literal verbal or auditory content experienced at the time of the traumatic event. In contrast, the second pathway proposes that some trauma-related auditory hallucinations are not directly linked to trauma memory intrusions, but instead

represent auditory images shaped by beliefs about the self and others abstracted from traumatic events and stored in autobiographical memory. They are also influenced by regulation strategies developed as survival mechanisms during trauma, such as dissociation, experiential avoidance, and hypervigilance, given the impact of these processes on sensory-perceptual processes. The findings here provide some tentative support for the existence of two pathways from trauma to auditory hallucinations, perhaps characterised by different levels of content links. Firstly, Study One did find that trauma memory intrusions had much stronger associations with auditory hallucinations for the small group who were rated to have direct links between their auditory hallucination content and the index traumatic event. Secondly, Study Three indicated that imaginal exposure acted to decrease the intrusiveness and sensory-perceptual quality of the trauma memories, and impacted on the severity of auditory hallucinations, possibly most effectively for those with direct content links. This provides support for the role of intrusive trauma memories in some auditory hallucinations, and the suggestion that this may be most relevant for those with direct content links. The fact that individual response to imaginal exposure was quite variable and that those with no direct (thematic) links between their auditory hallucinations and their trauma history appeared to show more limited response to this therapy also fits with the potential existence of a second pathway between trauma and auditory hallucinations, in which trauma memory intrusions are less implicated and other posttraumatic processes such as emotion regulation and schematic beliefs are primary. This assertion is based on the assumption that imaginal exposure primarily acts through elaboration (contextualisation) of the trauma memory and reduction of the intrusive nature of trauma memories; if imaginal exposure reduces auditory hallucinations, these auditory hallucinations might be deemed to be related to

decontextualised intrusive memories. The mechanisms involved in imaginal exposure are not clear cut. It is also posited that a key mechanism of change in imaginal exposure is changes in negative posttraumatic beliefs (Cooper et al., 2017). Study Three found medium effects on negative posttraumatic beliefs, indicating that this may indeed have been a contributing process of change in the present study. It thus appears that routes from trauma to psychosis are not as clear-cut as two specific pathways and perhaps trauma memory intrusions, emotion regulation, and beliefs are implicated to differing degrees for different people. The variability of response to the intervention may also suggest that some of the participants did not fall into either of the pathways linking trauma and auditory hallucinations in Hardy's (2017) model, but in fact represent a group for whom trauma is not linked to their auditory hallucinations.

Study One found that avoidance and hyperarousal did not have momentary associations with the occurrence of auditory hallucinations. This is in contradiction Hardy's (2017) proposal that attempts to regulate emotion (including experiential avoidance and hypervigilance to threat) are involved in the genesis and maintenance of auditory hallucinations following traumatic events. This finding is also in contrast with previous cross-sectional findings that posttraumatic avoidance and numbing, and hyperarousal, mediate the relationship between trauma and auditory hallucinations (Hardy et al., 2016; Powers et al., 2016). It is possible that the discrepancy in this finding relates to differences in momentary 'state' level associations and those at a 'trait' level. It may be that a trait tendency to avoidance and hyperarousal may be linked to the presence auditory hallucinations, but this is not clearly seen in moment-to-moment fluctuations. Or it may be that differences in measurement between Study One and these previous studies may have contributed to different findings. Study One

used DSM-5 criteria to measure avoidance, so may not have captured aspects of avoidance such as numbing and dissociation that were captured in these previous studies (and are implicated in Hardy's theory). Additionally, the item measuring hyperarousal in Study Two may not have effectively captured hypervigilance to threat, which is also theorised to be of importance (Dodgson & Gordon, 2009).

12.3.4 Imaginal exposure versus other trauma-informed or trauma-focused therapies used for auditory hallucinations

The pilot treatment study undertaken in Study Three is now the third pilot study of trauma-focused psychological interventions specifically for auditory hallucinations. The intervention used differed in important ways from the interventions delivered by Paulik et al. (2019) and Keen et al. (2017). As the only trials that have specifically treated auditory hallucinations using trauma-focused approaches, exploring the differences between these trials and the potential impact that these differences had on the results will be useful for informing the development of therapies in this area.

Keen et al. (2017) used an integrated trauma-focused therapy to treat both PTSD and psychotic symptoms in a case series (n=9). The therapy was a 'phase based' approach, which included 1) assessment, engagement and goal setting, 2) stabilisation and coping strategy enhancement, 3) formulation, and 4) integrated psychosis and trauma-focused interventions (including cognitive restructuring, imagery rescripting, reliving with cognitive restructuring and schema work). Participants received a median of 41 sessions (range 25-66). Notably, this study only delivered exposure-based memory work for memories that were related to PTSD intrusions and used cognitive restructuring to address auditory hallucinations. The study had no dropouts from therapy and no participants had a reliable worsening of

symptoms. In terms of auditory hallucination outcomes, five of nine participants had reductions on the PSYRATS-AHS at post treatment, with two of these showing reliable change (reductions of more than 9.76 points). The mean change in the PSYRATS-AHS between baseline and post treatment was 9.06 points. The pattern of findings in this study are similar to those found in Study Three, with a small number of people showing a large response to the therapy and the overall effect being of a similar magnitude. This finding may indicate that memory exposure work is not as central to therapy response as has been suggested in this thesis, since this study did not include trauma memory exposure work for traumatic events related to the auditory hallucinations. It should be noted that the median number of therapy sessions used by Keen et al. (41) far exceeds that used in this study (six), which may indicate that imaginal exposure is a more potent and 'efficient' way of achieving similar effects. This has to be balanced with the tolerability of the intervention. None of the participants in Keen et al.'s study discontinued therapy, which may have been due to the phase-based approach used, which emphasised safety and stabilisation prior to trauma memory processing work.

Paulik et al. (2019) report results from an imagery rescripting intervention specifically targeting trauma memories related to auditory hallucination content. In a case series design, 12 participants with auditory hallucinations that were thematically related to past trauma undertook an eight session imagery rescripting intervention. Imagery rescripting is a trauma-focused therapy in which the client is guided to imagine alternative endings to their trauma memories in which their needs are met. Imagery rescripting involves a degree of exposure to the trauma memory, but does not involve direct exposure to the most distressing aspects of the memory (the rescript begins before the most distressing aspect of the memory). This study used the distress

and frequency subscales of the PSYRATS-AHS to measure outcomes, finding medium to large reductions in distress and frequency ($d= 0.74$ and $d= 0.80$ respectively). The intervention was also well tolerated, with only one person dropping out of therapy (and this was because the person felt they had improved already). The small numbers and large confidence intervals in both the Paulik et al. study and in Study Three suggest that caution must be taken in comparing the magnitude of effects; however, the results indicate that imagery rescripting was a more tolerable therapy, but perhaps had slightly less potent effects on auditory hallucination outcomes. This again highlights the importance of balancing tolerability with potency when considering trauma-focused work for trauma-related auditory hallucinations. Approaches such as that used by Paulik et al. and Keen et al. that involve less direct exposure to the trauma memory may be more tolerable, but we might speculate based on comparisons of these results that these approaches, could be less potent.

12.3.5 The feasibility and acceptability of exposure-based trauma-focused therapies

The feasibility and acceptability findings of Study Three should be considered in the context of the wider literature regarding the general feasibility and acceptability of these therapies in PTSD populations as well as PTSD in psychosis populations. Firstly, it is well documented that real-life delivery of evidence-based trauma-focused therapies for PTSD is low. Becker et al. (2004) surveyed psychologists and found that less than 20% were using evidence-based trauma-focused therapies when treating PTSD. Respondents reported that fears about symptoms exacerbation and client dropout impacted on their decision to use trauma-focused therapies. This mirrors the low referral rates into Study Three, possibly due to clinician concerns about exposure-based therapies. It is also in line with research regarding the use of trauma-focused

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therapies in an early intervention service that found that clinicians were reluctant to deliver these therapies due to concerns about symptom exacerbation and safety (Gairns et al., 2015). This indicates that the issues with implementation identified in Study Three are not specific to the delivery of these interventions to treat psychotic symptoms, but are a more general implementation issue, in keeping with the wider literature relating to the use of trauma-focused interventions.

Another issue with feasibility in Study Three was the rate of dropout from therapy. Although based on small numbers, it is of note that the dropout rate of 27% is largely in line with the delivery of these therapies in general PTSD populations and in psychosis populations. A review of 25 randomised controlled trials of evidence-based trauma-focused therapies for general PTSD populations found dropout rates to be between 20-27% (compared to 11.4% in active control therapies such as supportive counselling; Hembree et al., 2003). Van den Berg et al. (2015a) also reported a therapy dropout rate of 22 % when using trauma-focused therapy for PTSD in psychosis populations.

Client uptake of imaginal exposure was also low in Study Three, with 43% of those who showed an interest in receiving a trauma therapy declining to participate when imaginal exposure was described to them. This is also in keeping with literature regarding client preferences for PTSD therapies, with one study of 110 people seeking treatment for chronic PTSD finding that participants showed a stronger preference for interpersonal therapy and that 26% of people indicated that they would not want to receive PE (Markowitz, Meehan, Petkova, Zhao et al., 2016).

Study Three also highlighted some potential issues with the acceptability of exposure-based trauma-focused therapies for auditory hallucinations. Although participants who completed therapy were generally satisfied, 25% did report

experiencing unmanageable distress in the sessions. Additionally, three people dropped out from therapy and reported this to be due to symptom exacerbation and distress. This is in contrast with van den Berg et al.'s large trial of PE and EMDR for comorbid PTSD in people with psychosis, which did not find significant exacerbation of psychotic or PTSD symptoms (van den Berg et al., 2015b). The difference between this study and Study Three may be an artefact of the different focus of therapy (trauma-related auditory hallucinations rather than PTSD), or to differences in participant characteristics or their service contexts. Only 40% of participants in van den Berg's study had active auditory hallucinations, whereas all participants in Study Three had current persistent and distressing auditory hallucinations. In line with the findings of Study Three, temporary symptom exacerbation in early sessions of PE has been reported in general PTSD populations (Larsen et al., 2016), and in an early psychosis population after talking about trauma (Tong et al., 2017). In contrast, these studies did not find early symptom exacerbation to be related to dropout or to worse outcomes in therapy, whereas the participants in Study Three did report that they discontinued therapy due to distress and symptom exacerbation. A qualitative study that more explicitly explored reasons for dropout from PE in a veteran population found that the therapy being 'too stressful' was a commonly cited reason (Hundt et al., 2018). Although there are some discrepancies relating to levels of symptom exacerbation in trials of PE, the findings from Study Three do suggest that symptom exacerbation and distress may be pertinent to cessation of treatment when working with trauma that is associated specifically with active psychotic symptoms, possibly due to reduced ability to tolerate this temporary increase in symptoms for some people with active auditory hallucinations.

12.3.6 Remission in trials of psychological therapies for auditory hallucinations

Two participants in Study Three had full remission from auditory hallucinations at one month follow up. This is of potential clinical significance when considering the chronicity of auditory hallucinations in the included sample (mean 19.7 years, SD 10.67). Other studies of trauma-focused psychological therapies have also reported total remission from auditory hallucinations. Paulik et al. (2019) reported one participant who experienced full remission from auditory hallucinations following their imagery rescripting intervention (this participant was the only participant in the study who had a direct content link between their auditory hallucinations and their trauma history), and van den Berg and van der Gaag (2012) reported that five out of eight participants who had active auditory hallucinations in a pilot study of EMDR to treat PTSD in people with psychosis no longer had auditory hallucinations at the end of the therapy. Given that these studies are uncontrolled, it is not possible to ascertain whether remission in auditory hallucinations was related to the interventions delivered, or whether this is an artefact of spontaneous remission. The largest randomised controlled trial of a psychological therapy for auditory hallucinations, the COMMAND trial did not provide data regarding instances of remission from auditory hallucinations and the AVATAR trial (Craig et al., 2018) reported that eight people in the treatment group and six people in the usual care group experienced remission from auditory hallucinations. Focussing on 'extreme responders' to a therapy, such as those who experience full remission from auditory hallucinations may be useful in understanding which therapies work best for whom and in unpicking the exact causal mechanisms involved in different people's auditory hallucinations.

12.4 Critical review of the empirical studies

The design and methods of the research studies were informed by relevant literature, guidelines, and consultation with expert researchers and experts by lived experience. Overall, the research was designed to provide the most robust assessment of the thesis aims within the constraints of the timeframe and resources available in a PhD program. The resulting research makes a valuable and novel contribution to the area of trauma-informed models and treatments of auditory hallucinations. There are some limitations that need careful consideration to provide a balanced interpretation of the findings. Key limitations of each of the three studies were highlighted in the relevant peer reviewed articles, but will be explored in more depth here.

12.4.1 Critical review of Study One

A strength of Study One was the novel use of EMA to provide innovative data regarding the dynamic moment-to-moment relationship between trauma memory intrusions, hyperarousal, and avoidance, and auditory hallucinations; however, a critical reflection on the study methods highlights several limitations.

Temporal ordering

Firstly, although Study One utilised a micro longitudinal approach, in which participant experiences were sampled repeatedly over a short time frame, the findings are still limited in informing temporal inferences. As highlighted in Part I, one of the key indicators of a causal relationship between two variables is temporality in the relationship. For a variable to be considered to have a causal role it needs to be established to temporally precede the outcome of interest. In EMA research, lagged relationships between a predictor variable and an outcome are the most informative regarding temporality. In the lagged model, it is clear that the predictor is influencing the outcome at the next time point, thus indicating a causal relationship. The

significant main effect of trauma memory intrusions found in Study One was only found at the proximal time point (i.e. a significant association between trauma memory intrusions and auditory hallucinations within the same time point). There were no significant main effects in the lagged model. This means that it is difficult to infer the nature of the association between trauma memory intrusions and auditory hallucinations. The wording of the EMA items means that trauma memory intrusions were being rated 'since the last beep' and auditory hallucinations were being rated 'just before the beep', suggesting that trauma memory intrusions are preceding auditory hallucinations, but precluding definitive conclusions about this. As discussed in section 7.1.5, there was a clear rationale behind wording the items in this way (based on the predicted frequency and phenomenology of the experiences); however, this does impact upon the interpretation of the results. It is also of interest to consider inferences regarding temporality in the relationship between trauma memory intrusions and auditory hallucinations in the context of theory in the area. Specifically, models have suggested that some auditory hallucinations are in fact a form of trauma memory intrusion (Hardy, 2017; Steel et al., 2005). Thus, theory might suggest a momentary relationship, rather than trauma memory intrusions temporally preceding auditory hallucinations per se. The results of Study One would therefore be in line with these theories, even though it is not possible to infer temporal relationships from the data. Given that theory implies more momentary associations between PTSD symptoms, it is possible that the time frames used to assess experiences in Study One were not an appropriate length to capture this. To reduce participant burden, beeps were at least half an hour apart, but it might be necessary to sample experiences at shorter intervals to capture the exact temporal relationship between PTSD symptoms and auditory hallucinations, for example sampling symptoms every 10 minutes, or

even less. It is likely that this sort of intensive sampling may lead to more reactivity and higher rates of missing data due to participant fatigue (Kimhy et al., 2012). One statistical analysis approach that may unpick the direction of relationships between variables is to reverse the variables in the analysis. Thus, confirming whether there is a unidirectional relationship, or whether the relationship is bidirectional and one of association, rather than causality. Given there were no main effects in the lagged analyses, undertaking reverse order analyses of these models was not indicated. Reverse order analyses were also not possible in the proximal analysis because the wording of the items precluded this; PTSD symptoms were measured 'since the last beep' and auditory hallucinations 'just before the beep', meaning that the direction of the relationship between these variables could not be reversed when measured within the same time point.

EMA items

The items used to measure variables in EMA studies have a large impact on the robustness of the findings. The findings of Study One may be limited by the use of single items to measure complex constructs. The PTSD symptom EMA items aimed to capture multifaceted experiences. For example, the trauma memory intrusion item did not capture a full range of re-experiencing phenomena (including, for example physical and emotional reactivity to reminders) that may be hypothesised to be related to auditory hallucinations. Theory suggests that auditory hallucinations may be a type of trauma memory intrusion that is decontextualised to the point that there is no recognition that it is a memory (Hardy, 2017; Steel et al., 2005). Thus, physical and emotional reactivity to reminders might be more recognisable to participants, whereas identifying intrusions as trauma-related memories might be less likely in this group. The hyperarousal item used was also potentially problematic; assessing the extent to

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which people felt alert, on edge, irritable, or jumpy may have conflated different aspects of hyperarousal and not have captured hypervigilance (heightened attention to threat) sufficiently. Hypervigilance, rather than hyperarousal, is implicated in relevant theory (Dodgson & Gordon, 2009; Hardy, 2017). Finally, the item used to measure the impact of posttraumatic avoidance was based on the DSM-5 conceptualisation of this symptom, which focuses on avoidance of thoughts and reminders of the event. This meant that other aspects of experiential avoidance that may have been important, such as dissociative and numbing responses (which were included in DSM-IV conceptualisations of posttraumatic avoidance in PTSD), were not captured. The results of Study One would likely have been strengthened through the inclusion of multiple EMA items to measure re-experiencing, avoidance, and hyperarousal, thus providing more comprehensive and robust measurement of the constructs of interest. This was not possible within the context of this thesis since the EMA schedule was delivered as part of a wider research study (Study Three) for many participants. Study Three already had a broad range of assessments included and it was deemed to be too burdensome to introduce multiple additional EMA items within this context.

Confounding variables

There are a number of variables that may have been confounds in the identified relationship between trauma memory intrusions and auditory hallucinations in Study One. For example, negative affect, paranoia, and activated negative schematic beliefs are all likely to be associated with both trauma memory intrusions and with auditory hallucinations. Since these experiences were not measured and controlled for as variables in Study One, it is not possible to discount their impact on the results. For example, it is plausible that general negative affect increases the

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chance of both trauma memory intrusions and auditory hallucinations and therefore underlies any association observed. The importance of accounting for confounding variables when examining causal mechanisms in psychotic experiences has been identified by researchers in the field (Bentall, 2003; Varese & Bentall, 2011). An example of the importance of confounding variables can be seen in a meta-analysis of the role of meta-cognitive beliefs in hallucinations, in which a moderate association was found in clinical groups, but when confounding variables (e.g. anxiety, depression, and paranoia) were controlled in the analysis, there was only a weak association (Varese & Bentall, 2011). As outlined in the previous section, the inclusion of additional EMA items in Study One was limited by the context of the study (embedded within the pilot treatment study that involved multiple assessments already) and the necessity to limit participant burden. The need for a further, more robust, EMA study to replicate the results of Study One is highlighted in more detail in section 12.6.

Sample size and power

There was no formal sample size calculation conducted for Study One. Due to the complexities of sample size calculation in multilevel models, Kreft's 30/30 rule of thumb was used (Kreft, 1996). Once participant attrition and missed data points were accounted for, Study One achieved an average of 42.5 data points per person, with 28 people included. While Kreft's rule of thumb has been widely used, it has since been demonstrated that the number of level one units (participants) is one of the most important determinants of statistical power in multilevel models (Bolger & Laurenceau, 2013). As such, the large average number of data points for each participant may not have resulted in substantial increases in power to detect effects, given the relatively small number of participants. Additionally, although the primary

focus of the study related to level one effects (i.e. average effects across participants) and simulation studies have indicated that Kreft's 30/30 rule of thumb is appropriate in this circumstance, the moderator analyses in Study One were examining between-person effects, which are likely to need a higher number of level two units (participants) to have sufficient power (Hox, 2010b). As a result, the moderator analyses may not have been sufficiently powered. Within the time constraints of the PhD there was little that could be done to mitigate issues with small sample size. The population of interest in the study was challenging to recruit, despite significant efforts to promote the study widely in relevant forums.

Generalisability

Another limitation of Study One relates to the specific selection criteria. The fact that Study One was partially embedded within Study Three led to a requirement for participants to have made a conceptual link between their auditory hallucinations and their trauma history. It should be noted that no one was excluded from participation based on this inclusion criterion; however, it is likely to have impacted on the characteristics of the sample because only those who had made this link will have put themselves forward for the study. This may limit the generalisability of the results of Study One since the group who have auditory hallucinations, have experienced trauma, and make a conceptual link between these experiences are likely to not be representative of the larger population with auditory hallucinations, or even of the population with auditory hallucinations and a trauma history. Many people with auditory hallucinations and a trauma history do not report an obvious link between these two experiences.

The potential selection bias introduced by only including people who have identified links between their auditory hallucinations and traumatic events may also

have inflated the associations found between posttraumatic stress symptoms and auditory hallucinations. People who have themselves identified these links may be more likely to endorse the presence of posttraumatic stress symptoms when endorsing the presence of auditory hallucinations because this is in keeping with their model of understanding of their experiences. Similarly, this group may also actually have greater associations between the two constructs, which has led to them making the link.

Nevertheless, this lack of generalisability and selection bias does not necessarily diminish the utility of the findings. Indeed, the lack of generalisability of the findings could actually be seen to be a strength of the study. It has been suggested that auditory hallucinations are not a single construct with one underlying cause, but are more likely to consists of subtypes that have distinct (but probably overlapping) causal pathways (McCarthy-Jones et al., 2014). Research that isolates specific subtypes of auditory hallucinations may be more likely to identify causal mechanisms that are relevant to this specific group of people, thus providing information for tailoring treatment approaches that target specific causal mechanisms (Smailes et al., 2015). A challenge that remains is identifying and clearly operationalising these subtypes of auditory hallucinations. Approaches that are able to disentangle between-person factors that moderate the causal impact of different mechanisms, such as that used in Study One, may represent a significant way forward in this endeavour.

Managing serial autocorrelation

A complexity in analysing time series data, such as EMA, is that data points that are closer together in time are likely to be more correlated that those that are further apart. When random time-based sampling is used, this is further complicated by data points that are of varying distances apart (and therefore vary in their likely

correlations). This phenomenon is termed serial autocorrelation. In Study One the potential for serial autocorrelation was managed by including the lagged (t-1) dependent variable in all models as a covariate. This has been suggested as an appropriate way to manage serial autocorrelation, particularly when data points are not evenly spaced (Raudenbusch et al., 2011). It should be noted that this practice has also been criticised, suggesting that it can lead to underestimations of coefficients for independent variables in the model (Keele & Kelly, 2017). Alternative methods for managing autocorrelation when there are unequal spaces between data time points have been suggested. Using a standard first order regressive AR(1) structure in this situation is not appropriate since it assumes equally spaced time points. Bolger and Laurenceau (2013) outline a spatial power error structure method available in SAS that adjusts for the length of time between data points. This approach is not available within the HLM-7 software and was therefore not used in the analysis for Study One.

12.4.2 Critical review of Study Two

Study Two was a preregistered and rigorously conducted systematic review and meta-analysis. The study was carried out in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines. These design elements aimed to ensure that the study findings were robust; however, some aspects of the retrieved studies included in the meta-analysis do have implications for the conclusions that can be drawn.

Number of studies included

Firstly, although the meta-analysis included 12 studies overall, only five controlled studies were available, which meant that the between-groups (controlled) analyses only included two to five studies (depending on the outcome being analysed). It has been highlighted that the number of studies included in a meta-

analysis is of importance when conducting random effects analyses. For example, it has been suggested that five or more studies are needed to achieve sufficient power for a random-effects meta-analysis (Jackson & Turner, 2017). This may have had impact upon the auditory hallucination and delusions outcome analyses, since there were only two controlled studies available. There are now a number of additional studies being undertaken that examine the effects of trauma focused therapies for people with psychosis, thus in the future a larger meta-analysis may be possible.

Quality of included studies

Confidence in the effect sizes and confidence intervals produced by meta-analyses can be heavily influenced by the level of bias of included studies and the overall quality of the body of evidence for each outcome. This has been termed the 'garbage in – garbage out' problem (Borenstein, 2009). In Study Two the risk of study bias was assessed using the Cochrane Risk of Bias Tool (Higgins & Green, 2011) and the quality of the body of evidence for each outcome assessed using the GRADE quality tool (Guyatt et al., 2008). These assessments indicated that only five individual studies were considered to be low risk of bias, and highlighted issues with consistency and precision that meant between-group effect sizes for negative symptoms and hallucinations post treatment, and for depression at both time points, were rated as low or very low confidence. This limits the findings in relation to these outcomes and indicates that higher quality evidence, taken from studies with lower risk of bias, is needed to provide more robust effect sizes for these outcomes.

12.4.3 Critical review of Study Three

The use of a single arm pilot study

Study Three was initially designed as a randomised controlled pilot study, yet slow recruitment meant that this was not feasible and the design was switched to a

single arm, open pilot trial. Given that this was the first study to examine the acceptability, feasibility, and potential effects of an exposure-based trauma focused intervention for auditory hallucinations it was considered that a single arm study would still be sufficient to provide useful data relating to the thesis aims; however, the use of a single arm study does lead to some limitations. Effect sizes in uncontrolled, within group studies are likely to be inflated in comparison to controlled, between-group studies (Schäfer & Schwarz, 2019). The lack of a control group means that it is not possible to control for natural changes in experiences over time, or of regression to the mean (i.e. in this situation, people selected based on having severe auditory hallucinations are statistically likely to show a reduction in their scores toward the mean just by virtue of the severity of their symptoms). It also means that investigator bias is more likely to impact upon outcomes. Although the follow-up interviews were conducted by independent research assistants who had not been involved in the participant's intervention, these interviewers were aware that everyone they assessed had received the intervention (due to there being no control group) so it is possible they would be more inclined to 'down rate' symptom severity based on this. Thus, it is likely that the effect size estimates for the effectiveness outcomes are over-estimations of those that would be seen in more robust controlled studies.

Small sample size

Pilot trials are generally not powered to assess the statistical significance of effects due to small sample sizes. The aim of a pilot trial is usually to primarily assess feasibility and acceptability and to provide an initial estimation of effect sizes (Lancaster et al., 2004), as such there are not clear guidelines for appropriate sample sizes. The sample included in the calculation of effect sizes and confidence intervals for Study Three consisted of 12 participants for whom there were available data.

Because of this small sample size it was appropriate for Study Three to focus on the estimation of effect sizes and their confidence intervals, rather than on statistical testing (Lee et al., 2014). The small sample size is also likely to have impacted on the estimation of confidence intervals, since 95% confidence intervals are still based upon the traditional 5% significance threshold (which this study was not powered to detect). When studies are underpowered this can result in Type II errors (in which the study concludes that there is no effect when there is in fact a true effect). In pilot treatment studies it is important that Type II errors are avoided, since a Type II error can mean that potentially effective treatments are not pursued. Lee et al. (2014) have recommended that pilot trials investigate confidence intervals of different widths to inform decision making, balancing the ramifications of Type II errors against the alternative Type I error (in which the study concludes that there is an effect when there is in fact no true effect). Thus, confidence intervals of 90% and 80% can be calculated and used to inform decisions about future definitive trials. In the case of Study Three this may have been a more informative approach than solely using a 95% confidence interval. This is important when considering the main outcome in which the 95% confidence interval narrowly crossed zero but would not have done so had a more liberal confidence interval been calculated.

Selection criteria

A further potential limitation of Study Three is that of external validity. The use of a brief exposure-based trauma-focused therapy (that required people to have a target index trauma memory and begin exposure in session two) and the need to measure PTSD symptoms in relation to an auditory hallucination-related trauma necessitated participants to have already made some conceptual links between their trauma history and their auditory hallucinations prior to entering the study. The

effectiveness estimates can perhaps therefore be seen as a proof of concept (i.e. indication that exposure-based trauma-focused interventions can have an impact on auditory hallucination severity); however, the specific sample used in this study may preclude the generalisation of these results to a wider population of people with auditory hallucinations. The selection criteria used in the study reflect a wider issue in the field relating to the operationalisation and identification of people for whom posttraumatic stress symptoms and trauma memory processing are of relevance to their auditory hallucinations. It is clear that the intervention used in Study Three will not be of relevance to all people with auditory hallucinations. Not all people who have auditory hallucinations have experienced traumatic events, and posttraumatic stress symptoms may not be a causal mechanism for all people who have auditory hallucinations and have experienced trauma. As has been posited by researchers in the field, it is likely that there are a number of subtypes of auditory hallucinations with different causal pathways involved (McCarthy-Jones et al., 2014) and these subtypes are likely to show differential responses to treatments that target specific causal mechanisms (Smailes et al., 2015). A challenge in the field is to identify subgroups to test targeted treatments. The narrow selection criteria for Study Three can also be seen as a strength since this study provides one of the first attempts at targeting a psychological therapy for auditory hallucinations to a specific subgroup. Further work needs to be done to refine this approach and ensure more sophisticated identification of subgroups for whom specific mechanisms are of relevance. The field may benefit from drawing on the approach taken by Freeman et al. in their development of targeted psychological therapies for specific causal mechanisms involved in paranoia. In this approach, decisions relating to which treatment modules to deliver to an individual are based both on formal assessment of the presence of difficulties in each

area (sleep, worry, avoidance, low self-esteem, and reasoning biases) and on client preference. Thus, formulation for a particular client involves the identification of empirically derived psychological mechanisms that may be of relevance for that individual, and the selection of which areas to focus on is driven by the client's own preferences and understanding of factors that are of relevance in their difficulties (Freeman, Bradley, et al., 2016; Freeman, Waite, et al., 2016). The approach taken in Study Three is somewhat similar to this approach since the aim was to ensure that participants were receiving a therapy that they felt was of relevance to their difficulties.

Comparing EMA auditory hallucination outcomes (and the need for further examination of distress and frequency outcomes)

Study Three utilised EMA ratings of auditory hallucination intensity and distress in addition to the PSYRATS-AHS as a primary effectiveness outcome measure. This was due to our concern that the PSYRATS-AHS might not be sensitive enough to detect more subtle effects on auditory hallucinations. Although not yet widely used as an outcome tool in psychological treatment trials, EMA has been suggested to provide a more sensitive measure of symptom outcomes for clinical trials, subject to less retrospective bias (Verhagen et al., 2016). The innovative use of EMA as an outcome measure is a strength of Study Three. EMA has not been widely used as an outcome measure in psychological treatment trials, so there is little data regarding how EMA results are likely to relate to standard retrospective reporting outcome measures. Although the small sample size and wide confidence intervals preclude precise comparisons of changes on EMA measures of auditory hallucinations and changes on the PSYRATS-AHS, the effects seen on some EMA items for auditory hallucinations were estimated to be of a larger magnitude than those seen on

the PSYRATS-AHS (the effect size for the PSYRATS-AHS post treatment was, adjusted d = 0.41 and the effect size for the auditory hallucination distress item post treatment was adjusted d = 0.74). The potential finding of increased sensitivity in measuring outcomes is in keeping with a randomised controlled trial of mindfulness for depression in an older adult population that reported greater effects on EMA ratings of depression than on standard retrospective self-report questionnaires of depression (ref Moore). Further research is needed to understand the sensitivity to change of EMA measures of auditory hallucinations, and how this might relate to standard retrospective measures.

Though based on a small sample (n=10) and providing imprecise effect sizes (with wide, overlapping confidence intervals), it is of note that the EMA measures indicated greater effects only on the auditory hallucination related distress item (adjusted d = 0.74) , with the intensity item showing only a minimal effect (adjusted d = 0.08). It is not possible to draw definitive conclusions from this finding; however, it does indicate that there may be a need to examine effects on different dimensions of auditory hallucinations (i.e. frequency and distress) to understand exactly what is changing. Analyses of the frequency and distress subscales of the PSYRATS-AHS were not included as preregistered analyses for Study Three and due to the small sample size, it was decided that a post hoc analysis of the subscales of the PSYRATS-AHS would not be indicated. Analysis of large numbers of outcome variables in studies with small sample sizes can increase the chance of spurious findings. This means that a comparison of the EMA distress and frequency items with their corresponding PSYRATS-AHS subscales was not conducted as part of Study Three. It would be of interest to examine this in future research with larger samples.

Examining specific mechanisms using complex treatments

Study Three aimed to deliver a specific intervention component hypothesised to act on precise causal mechanisms (posttraumatic stress symptoms and trauma memory processing). This was to assess the possibilities of this intervention as therapeutic tool, but also to provide initial data regarding the role of these putative causal mechanisms in auditory hallucinations (in the spirit of an interventionalist causal framework). In reality, imaginal exposure (as delivered in the PE manual) may involve a number of active therapeutic ingredients, including a warm validating therapeutic relationship, contextualising the trauma memory, habituation to the trauma memory, and cognitive restructuring of negative posttraumatic beliefs. Thus, it is difficult to disentangle which specific components may have led to the effects observed on auditory hallucinations. These therapy components also potentially act on a range of putative causal mechanisms, thus complicating conclusions about mechanisms of action of the intervention as well as in identifying causal mechanisms involved in auditory hallucinations. Although the inclusion of process measures in Study Three provided some insight into the mechanisms of action of the treatment, these measures indicated that the intervention acted on several mechanisms, and it was not possible to examine which of these mediated improvements in auditory hallucinations. As will be discussed in section 12.6, this will need to be explored in future research using well powered designs with more sophisticated analyses.

The use of a transdiagnostic sample

As described in section 7.3.3, Study Three took a transdiagnostic, symptom-specific approach. This was based on previous literature indicating that auditory hallucinations are common across a number of different diagnostic categories and that there are no clear differences in the phenomenological characteristics of auditory

hallucinations between people with different diagnoses (Larøi et al., 2012; Waters & Fernyhough, 2017). Additionally, it has been argued that symptom-specific, rather than diagnosis-based, approaches to psychological treatments for psychosis may improve efficacy, be more informative regarding specific mechanisms involved in auditory hallucinations, and may be more externally valid for clinical practice in which the reality is that people with distressing auditory hallucinations who seek treatment are likely to meet criteria for a range of diagnoses (Thomas et al., 2014). Including people with a range of diagnoses could leave Study Three open to a specific criticism in relation to the nature of the auditory hallucinations of those included. Specifically, it may be suggested that participants in this study did not have auditory hallucinations, but actually had posttraumatic re-experiencing symptoms (trauma memory intrusions). This is a complicated division to navigate, since it is clear that the lines of what defines an auditory hallucination are blurred, with the term actually encompassing a broad spectrum phenomenology of experience ranging from auditory imagery (mental representations based on auditory perceptions), to intrusive and vivid thoughts with a sense of 'otherness', through to more frank experiences of hearing complex sounds and voices (Jones & Luhrmann, 2016; Woods et al., 2015). It has also been suggested that posttraumatic stress symptoms and psychotic symptoms do not have a clear divide but may be on a spectrum of posttraumatic reactions with the cultural acceptability of the person's interpretation of the experience defining whether it is seen as PTSD or as psychotic (Morrison et al., 2003). Aside from these complicated conceptual issues surrounding the classification of psychotic and posttraumatic symptoms, it is clear that the final sample for the study did have experiences that would classically be considered to be 'psychotic' rather than purely a PTSD presentation. For example, the majority of the participants met diagnostic

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criteria for schizophrenia spectrum disorders. In addition, even though some of the participants had auditory hallucination content that was a replay of exact things heard at the time of the traumatic event, all of these participants also had additional auditory hallucination content.

12.5 Clinical implications and future directions

Findings from the three studies have implications for clinical practice, specifically in the development of trauma-focused interventions for auditory hallucinations. As highlighted in section 12.1.2 findings from all three studies indicate that trauma-focused interventions that focus on trauma memory processing and reducing trauma memory intrusions may be of use for treating trauma-related auditory hallucinations. The findings from Study One implicate trauma memory intrusions as having a momentary relationship with some auditory hallucinations, suggesting that intervening with these experiences may also impact upon some peoples' auditory hallucinations. Secondly, studies two and three provide indication that trauma-focused therapies can have an impact on psychotic symptoms, with Study Three providing a proof of concept that trauma-focused therapies that specifically target traumatic events linked to auditory hallucinations can have large impacts on auditory hallucinations. This is of significance since psychological interventions for auditory hallucinations are currently limited in their efficacy (Thomas et al., 2014). The predominant focus of psychological therapies for auditory hallucinations in recent decades has been on modifying power beliefs (a putative psychological mechanism in auditory hallucination-related distress, e.g. Birchwood et al., 2014). Developing therapies that focus on additional empirically supported psychological mechanisms can provide important new avenues in therapy development and create more evidence-based therapy options for people seeking treatment for distressing auditory

hallucinations. A focus on putative causal mechanisms is a diversion from recent psychological therapies for auditory hallucinations, since the aim of the intervention includes reducing the experience of auditory hallucinations themselves, rather than having a primary focus on reducing distress (which has been the main focus of psychological interventions for auditory hallucinations in recent decades). Based on clinical experience working with people with distressing auditory hallucinations this would seem to be in line with the goal of many (but not all) people seeking treatment. It is of note that the studies undertaken for this PhD can only provide preliminary estimates of the efficacy of trauma-focused therapies for trauma-related auditory hallucinations and this must be further assessed in more robust research trials prior to be considered as an evidence-based therapy for implementation in clinical practice. Nonetheless, apparent variability in therapy response and data regarding the acceptability and feasibility of the standard brief imaginal exposure intervention used in Study Three highlight three overarching considerations for the future development and delivery of exposure-based trauma-focused therapies in clinical practice: the tension between tolerability and potency, targeting trauma-focused therapies for trauma-related auditory hallucinations, and implementation issues. These will be addressed in turn.

12.5.1 The tension between tolerability and potency

Firstly, findings have highlighted a tension between delivering interventions that are tolerable and are also potent in their effects. Findings from Study Three indicate that imaginal exposure is generally acceptable when delivered as a standalone brief therapy, but that distress and symptom exacerbation are common and unmanageable for some people. It appears that it will be important to adapt the approach for some people to increase tolerability. This may involve preceding the

apparently 'potent' intervention of imaginal exposure with approaches that can develop contexts of external and internal safety, to increase people's resources to manage the potential distress and symptom exacerbation that may be experienced in the early stages of imaginal exposure. Some therapeutic models that may be of interest as helpful interventions prior to imaginal exposure work are compassion focused therapy, which is being piloted with people with distressing auditory hallucinations (Heriot-Maitland, McCarthy-Jones, Longden, & Gilbert, 2019). This focus on preparatory work prior to trauma memory exposure work would be in line with phase-based approaches to working with complex trauma that highlight the importance of a safety and stabilising phase of therapy prior to memory processing work (Herman, 1992). As yet, there is limited data regarding the superiority of this approach in terms of efficacy and tolerability for people with complex interpersonal trauma (De Jongh et al., 2016). Additionally, the data available in this PhD is not sufficient to infer whether this phase-based approach would be more tolerable when specifically using imaginal exposure for auditory hallucinations. The inclusion of complex PTSD in ICD -11 means that there is an increasing literature regarding the need to adapt (or not) standard trauma-focused therapies when working with this population. The diagnosis of complex PTSD aims to capture a constellation of symptoms that are common following traumatic events that are severe, prolonged, and repeated (and often interpersonal in nature). ICD-11 defines that people with complex PTSD meet criteria for PTSD, but also experience symptoms that are associated with disturbances *in self-organisation*, including affective dysregulation, negative self-concept and disturbances in relationships. Given that many people with auditory hallucinations have experienced prolonged and repeated interpersonal trauma, and that many of the mechanisms proposed to mediate the relationship between traumatic

events and auditory hallucinations overlap considerably with broader symptoms of complex PTSD (Williams et al., 2018), it may be of use to draw upon developing treatment guidelines for complex PTSD to inform the development of tolerable and potent interventions for trauma-related auditory hallucinations. An alternative approach to balancing tolerability and potency is to use trauma memory work that is less intensive than imaginal exposure. The PE protocol involves more direct exposure to the trauma memory than other trauma-focused therapies. Approaches such as Ehler's and Clark's cognitive therapy for PTSD involve exposure to the trauma memory, but this is generally a smaller proportion of the therapy session and is less prolonged and repetitive (Ehlers, Clark, Hackmann, McManus, & Fennell, 2005). Similarly, imagery rescripting is a less confronting approach that does not involve direct exposure to the trauma memory, but may be still facilitate trauma memory processing. This approach has shown promise as an acceptable, tolerable intervention for trauma-related distressing auditory hallucinations (Paulik et al., 2019).

12.5.2 Targeting trauma-focused therapies for trauma-related auditory hallucinations

The second issue arising from the results of Study One and Study Three relates to the potential need to target the use of trauma-focused therapies for auditory hallucinations to those who are most likely to benefit. Results from Study One indicated that there may be factors that moderate the association between trauma memory intrusions and auditory hallucinations, perhaps indicated by the presence of content links between the auditory hallucinations and the person's trauma history. This suggests that therapeutic approaches that target trauma memory intrusions will be most relevant and effective for a subgroup of people. Study Three also indicated variability in response to therapy, varying from total remission from auditory

hallucinations, to no response at all. Again, this suggests that the large effects of imaginal exposure on auditory hallucination severity were largely driven by the therapy being very effective for a small group of people. Additionally, the selection criteria for both Study One and Study Three were relatively restrictive in that participants were required to have made a link between their trauma and their auditory hallucinations. This was a necessary requirement for studying a brief imaginal exposure intervention and measuring its impacts on trauma memories that were of specific relevance to auditory hallucinations, however this also indicates that the relevance of trauma memory intrusions and of imaginal exposure interventions may be specific to this group of people. This is central in defining the populations who may benefit from these therapies in real world clinical practice. The publication presented in Chapter Eleven used two clinical case studies from Study Three to explore some of these issues, hypothesising that imaginal exposure may be most indicated when people have direct content links between their auditory hallucinations and trauma history and/or have concurrent related intrusive trauma memories. It is also significant to consider the fact that many people found brief imaginal exposure tolerable and acceptable, but that there were a small group of people who found the approach to be unmanageable. Identifying what might influence the tolerability of exposure-based trauma-focused therapies is also of importance for their safe delivery in clinical practice. While the numbers involved in the pilot study are too small to make definitive conclusions about this, the findings raise some potential factors that may be important to consider when deciding whether and when to undertake exposure-based trauma-focused therapies. There may be a need to consider the role that someone's persecutory appraisals of their auditory hallucinations may have on their ability to tolerate any exacerbation of their auditory hallucinations. If the

auditory hallucinations are considered to represent a current threat with high levels of conviction, then this may make increases in the experience overwhelming. Similarly, if people are living in circumstances in which they are (objectively or subjectively) unsafe, then this is likely to impact upon their ability to revisit and process traumatic experiences and to tolerate any temporary increase in PTSD symptoms or auditory hallucinations.

12.5.3 Implementation issues

The final issue that is of relevance for delivering exposure-based trauma-focused therapies in real world clinical practice relates to implementation issues. Some of the feasibility issues with researching exposure-based trauma-focused therapies are also likely to translate into issues with future implementation of the intervention in clinical practice. Even if a brief imaginal exposure intervention is found to be effective for some trauma-related auditory hallucinations, the slow referral rates into Study Three and the low uptake among eligible participants suggest that there may be both clinician and client reluctance to undertake such an intensive therapy. As discussed in section 12.3.4, this has been a general issue with implementation of exposure-based trauma-focused therapies for treating PTSD. Further research relating to client and clinician preferences and concerns relating to trauma-focused therapies for auditory hallucinations is needed to inform successful implementation, however it may be that exposure-based interventions may be more acceptable to clinicians and clients if they are embedded within broader trauma-informed approaches in which time is taken to build up a safe therapeutic relationship and to develop a formulation that provides a clear rationale for the use of trauma memory exposure, where indicated and based on client preference. There is also evidence that specialist training and supervision in the use of trauma-focused

therapies for people with psychosis has positive effects on credibility beliefs and perceptions of burden and harm concerning these treatments (van den Berg et al., 2016), suggesting that this will also be vital to support implementation in clinical practice.

As has been noted, results from the studies included in this thesis indicate that imaginal exposure is likely to be most relevant and effective for a small group of people: those who identify as having experienced traumatic events, and who relate these experiences to their auditory hallucinations, and who have (some) hallucinations that represent 'replays' of past traumatic material. Available data suggests that approximately 13% of people with auditory hallucinations who have experienced traumatic events auditory hallucination content that includes direct replays of trauma material (Hardy et al., 2005). While this limits the applicability of the intervention, the importance of developing therapies that target putative causal mechanisms involved in subtypes of auditory hallucinations has been identified as a way to improve overall efficacy (Smailes et al., 2015). In line with the tenets of personalised medicine, targeting therapies to those for whom they will be most effective can ensure that all people receive the treatment most appropriate for them. Arguably, even improving therapies for 13% of people with auditory hallucinations will have a worthwhile impact.

12.6 Research implications and future directions

There is a growing body of literature examining putative causal mechanisms involved in the link between trauma and auditory hallucinations, as well as an emerging literature relating to the use of trauma-focused therapies to treat psychotic symptoms. Since starting this PhD there have been two small pilot intervention studies using trauma-focused therapies to treat auditory hallucinations (Paulik et al., 2019; Keen et al., 2017), and there are now a number of larger trials underway that examine the effectiveness of trauma-focused therapies for PTSD in psychosis, as well as examining impacts on psychotic symptoms (e.g. Clinicaltrials.gov IDs: NCT03664713, NCT03991377; ISRCTN.com IDs: ISRCTN16262847, ISRCTN56150327). The findings of this thesis have implications for the development of research in this area and also point toward some key future areas of focus.

12.6.1 The next step in EMA research examining the relationship between posttraumatic stress symptoms and auditory hallucinations

The findings of Study One indicate that trauma memory intrusions have momentary associations with auditory hallucinations. While providing preliminary evidence regarding this relationship, there were a number of limitations in the design of Study One and the findings therefore need to be replicated in a more methodologically robust study.

Firstly, this relationship needs to be explored in a broader sample of people – perhaps focusing on a group who have auditory hallucinations and have a history of traumatic events but not requiring them to have made any links between these. A larger sample size will also ensure sufficient power to detect effects and to conduct robust moderator analyses. An extension to Study One will also be to include multi-item assessments of PTSD symptoms to provide more rigorous measurement and

allow for the disaggregation of effects between different symptoms within each symptom cluster, for example examining the specific effects of hypervigilance versus irritability in the hyperarousal symptom cluster. Additionally, in line with recommendations in the field (Bentall, 2003; Varese & Bentall, 2011), it will be important to include measurement of potential confounding variables, such as paranoia, negative affect, and activated negative schematic beliefs to partial out the confounding effects of these variables in the analysis. The findings from Study One also suggest that the impact of posttraumatic stress symptoms on auditory hallucinations may be a very proximal relationship, thus including shorter assessment timeframes may be required to disentangle the temporal ordering of these experiences (or ascertain whether they do indeed occur simultaneously). The sampling timeframe will still need to be balanced against participant burden and the risk of increasing reactivity to measurement.

12.6.2 A fully powered randomised controlled trial

Publication One (presented in Chapter Six) identified that the most robust and ethically feasible way to assess the role of posttraumatic stress symptoms in auditory hallucinations is to conduct a well-controlled trial of a trauma-focused therapy (known to act on the mechanisms of interest) for auditory hallucinations. The pilot study conducted in Study Three aimed to provide preliminary data to inform the development of such a trial. The findings from Study One do warrant a further investigation of an exposure-based trauma-focused therapy such as imaginal exposure to treat auditory hallucinations since the intervention was found to be generally acceptable and to have potentially large effects on auditory hallucinations. The findings do highlight some considerations in undertaking a larger randomised controlled trial. Firstly, the findings suggest that there may need to be some

adaptations to the intervention model to increase its tolerability. Thus, a future trial may need to embed the active exposure-based intervention within a broader trauma-focused therapy approach. The specific effects of different aspects of trauma-focused therapies could be assessed in a factorial design, in which different treatment components are introduced sequentially and the effects of each component individually assessed. This would allow for a specific analysis of the effects of exposure and therefore of the putative mechanisms of interest in this thesis.

There is also some evidence that other approaches that include exposure to the trauma memory, but are less intensive and confronting, might be fruitful interventions. Imagery rescripting has been found to have positive effects and to be tolerable for people with trauma-related auditory hallucinations (Paulik et al., 2019). Additionally, there is growing evidence that brief written exposure interventions may be as potent as standard trauma-focused therapies and shows lower dropout rates (Thompson-Hollands, Marx, & Sloan, 2019). The findings of Study Three also indicate the need to examine both moderators and mediators of change in a future randomised controlled trial. The fact that participants showed large variability in their response to the intervention in Study Three suggests that there may be a subgroup of people who respond particularly well to this intervention. To further identify who is most likely to respond to exposure-based trauma-focused interventions, it will be important to examine moderators in a sufficiently well-powered analysis. This will aid more targeted delivery of these therapies in the future. In line with the interventionist–causal approach it is also necessary to understand the mechanisms through which the intervention operates. The findings of Study Three were consistent with it operating on the hypothesised mechanisms of interest (the intrusiveness of trauma memories and trauma memory processing), but also found evidence of changes in other potential

mechanisms (negative posttraumatic cognitions). To fully examine the mechanisms involved in the intervention, and therefore understand the causal mechanisms involved in trauma-related auditory hallucinations, it will be important ascertain which mechanisms are in fact mediators of change in auditory hallucinations.

The findings of Study Three indicate a potential feasibility issue with conducting a large randomised controlled trial of exposure-based trauma-focused therapies for auditory hallucinations. Recruitment into the study was slow and few clinicians referred their clients into the study, despite widespread promotion. This suggests that it may not be feasible to recruit sufficient numbers for a larger trial with similar selection criteria and a comparable intervention. One solution could be broadening the inclusion criteria to not require people to have already made a link between their auditory hallucinations and their trauma history. This would also require embedding the imaginal exposure intervention in a broader trauma-informed CBTp approach (much like the approach taken by Keen et al., 2017) in which there is a phase in which any links between traumatic events and auditory hallucinations can be formulated collaboratively. One potential issue with this approach is that it is likely to not prove to be useful or relevant to reformulate every participant's auditory hallucinations as related to specific traumatic events. It is also possible that the intervention could be developed and adapted to be more attractive to potential participants and to referring clinicians (for example using the less confronting intervention approaches outlined previously). It may be that a large randomised controlled trial is not feasible regardless of changes made to the protocol. It may be that well controlled and robust methodologies that are appropriate for smaller sample sizes may be more feasible (and perhaps informative) methods to progress this research agenda.

12.6.3 Idiographic approaches

For the past few decades there has been an emphasis on nomothetic (group based) research as a gold standard in examining the efficacy of psychological therapies. The randomised controlled trial is the primary example of this. Using randomised controlled trials a therapy is considered to be efficacious if, following the intervention period, the average score of the treatment group is significantly lower than the average score of the control group. Individual differences in treatment response are not usually examined unless the study is sufficiently powered to examine characteristics that may moderate treatment response (using averaged values of smaller groups organised according to specific characteristics). Idiographic approaches on the other hand have a focus on change at an individual level. Thus, in this approach scores are not averaged across a group, but the focus is on how an individual's score changes throughout the treatment. There has been a recent increase in interest in idiographic research methods in clinical psychology research. Piccirilo, Beck and Rodebaugh (2019) outline what is known as *the therapist's dilemma* in which clinicians are primarily trained in nomothetic research methods but are then tasked with treating specific individuals using this group-based evidence. A desire to better evaluate how interventions work at an individual level (i.e. what works for whom and how) has fuelled increased interest in idiographic research methods. Additionally, there is now evidence to suggest that aggregated group-level data is concerningly imprecise at describing individual participants (Fisher, Medaglia, & Jeronimus, 2018). Methods that can provide intensive individual data, such as EMA, and analysis techniques that can model this data across time are also becoming more accessible to clinician researchers (Piccirillo et al., 2019), thus increasing the potential for these approaches. Single-case experimental designs (SCEDs) provide researchers

with a viable alternative to group designs. In contrast to group designs in which one group is compared with another, in a SCED a participant provides their own control data for a within-person analysis of the effects of an intervention. A SCED can determine whether a causal relationship exists between a manipulated independent variable and a meaningful change in the dependent variable of interest. SCEDS generally involve repeated measurements over time to establish changes that occur as a result of the intervention, and replication of this effect either within or between participants. There are now well-established methods to ensure robustness in the results of SCEDs (Smith, 2012).

Idiographic approaches such as the SCED may be a useful research methodology to extend upon the current thesis research. The variability of intervention response in Study Three suggests that individual level response may be more informative when examining causal relationships between trauma memory intrusions and trauma memory processing and auditory hallucinations. Additionally, the fact that the group for whom trauma memory intrusions and trauma memory processing may be of causal importance in auditory hallucinations is only a small subgroup means that recruitment to a fully powered randomised controlled trial may not be feasible. A SCED provides a robust methodology that does not require large sample sizes, thus making it a more feasible alternative. A SCED is also well placed to carefully examine the impact of multiple intervention components and the specific mechanisms of action of each intervention component. This would be an important extension on the research in this thesis, which suggests that multiple overlapping mechanisms may be at play, and that a multi component intervention that addresses a range of posttraumatic issues may be more feasible and acceptable to deliver.

For example, a number of participants with auditory hallucinations and histories of traumatic events could be recruited to receive a series of trauma focused intervention components, including: collaborative formulation of any links between trauma and auditory hallucinations, building a sense of safety using attachment imagery or compassion focused therapy, cognitive restructuring, and trauma memory exposure work. The intervention components would be sequentially delivered following a randomised period of baseline measurements (in which no intervention is delivered). Repeated measurements of the independent variables of interest (e.g. trauma memory intrusions, hyperarousal, avoidance, trauma memory processing, negative affect, and dissociation) could be taken using EMA and a network intervention analysis approach used (Blanken et al., 2019). Such an approach could model how relationships between these variables and the dependent variable (auditory hallucinations) change over time and whether this is different across the different phases of treatment. This would provide information to address the two aims of this thesis: the causal role of trauma-related processes in auditory hallucinations, and the effectiveness of trauma-focused therapies for auditory hallucinations. This approach would also allow for a more feasible (in terms of participant recruitment) assessment of the relative usefulness of different therapy components for people with different trauma-related processes involved in their auditory hallucinations (which this thesis has highlighted are necessary areas of enquiry in future research).

12.6.4 Exploring clinician and client perspectives and preferences

The findings of Study Three also highlighted the need for research that explores both client and clinician perspectives and preferences in relation to trauma-focused therapies. Understanding potential barriers to referring into or accessing these

treatments will ensure the design of more feasible trials and therapies that are more likely to have success at the stage of implementation into real world practice.

12.6.5 Developing a multicomponent therapy for auditory hallucinations based on empirically supported causal mechanisms

The findings of this thesis also highlight the potential for developing new therapy components for auditory hallucinations that are based on empirically supported mechanisms. It has been highlighted throughout this thesis that there has been relatively little psychological intervention development specifically for auditory hallucinations that is grounded in contemporary empirical evidence relating to putative causal mechanisms. The handful of treatment trials that have used this approach have mainly focused on one causal mechanism (beliefs about power and omnipotence) primarily thought to be involved in maintaining distress. Shifting focus to putative mechanisms that may be involved in the genesis of, or fluctuations in, auditory hallucinations may provide much needed improvements in efficacy. The approach taken in this thesis would be replicated and expanded as a model for exploring a range of potential causal mechanisms likely to be amenable to psychological interventions. Mirroring the approach taken by Freeman et al. (Freeman, Waite, et al., 2016), putative mechanisms might be identified through systematic reviews of the literature, further experimental studies or studies using EMA can test the role that these mechanisms may play. Then interventions that are designed to target these mechanisms can be piloted and scaled up into larger controlled trials (or examined in robust idiographic research where this is more appropriate). The ultimate aim would be to have a menu of effective intervention components that are then tailored to individuals based on formulated mechanisms involved in their auditory hallucinations and on client preference.

12.6.6 Understanding resilience and protective factors

One area that this thesis has not examined is that of resilience and protective factors. Many people who experience traumatic and adverse events in childhood do not go on to develop auditory hallucinations. Additionally, there is growing recognition that some people who experience traumatic events and develop auditory hallucinations are not distressed by these experiences and may in fact view them to be helpful ways of coping with difficult life circumstances. Understanding factors that may be protective against the development of auditory hallucinations following trauma and adversity, or that influence whether they are experienced to be adaptive and helpful may help to shed light on the processes involved in the genesis and evolution of distressing auditory hallucinations. An understanding of these factors may also help to develop prevention and intervention approaches.

12.7 Summary and conclusions

The program of research outlined in this thesis aimed to explore the role of PTSD symptoms and trauma memory processing as potential psychological mechanisms involved in auditory hallucinations, and as a potential target for treatment using trauma-focused psychological therapies. A multi methods approach was taken to address this aim, including an EMA study of the moment-to-moment relationship between PTSD symptoms and auditory hallucinations, a systematic review and meta-analysis examining the secondary effects of trauma focused therapies used to treat PTSD in populations with psychosis on psychotic symptoms, and a pilot treatment study examining the feasibility, acceptability, and potential effects of an exposure-based trauma focused therapy for trauma-related auditory hallucinations.

EMA findings suggest that trauma memory intrusions may have momentary associations with hallucinations and that this relationship is stronger and more

enduring for people who have auditory hallucination content that is directly related to the traumatic event. The meta-analysis suggested promising secondary effects of trauma-focused therapies on positive symptoms, but few studies examined auditory hallucinations specifically. Finally, the pilot therapy study found that a brief exposure-based trauma-focused therapy was generally acceptable but had low uptake. Symptom exacerbation and distress were common; most people found this tolerable, but a small number reported that this led to them ceasing therapy. There were large estimated effects on auditory hallucination severity, but individual response was highly variable. Visual inspection of session-by-session scores suggested that the intervention was effective for the group who had a direct link between their auditory hallucination content and their trauma.

Overall, these findings provide support for the theory that (some) auditory hallucinations are closely associated with trauma memory intrusions. Exposure-based trauma focused therapies may be an effective intervention for some people, but others may find the process of exposure difficult to tolerate. Further research is needed to definitively assess efficacy and to identify clinical and contextual factors that influence therapy response and tolerability.

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Appendices

Appendix I Ethical approval certificates

Swinburne Research

Authorship Indication Form
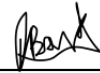
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DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Can we use an interventionist-causal paradigm to untangle the relationship between trauma, PTSD and psychosis?

First Author

Name Rachel Brand   Signature:

Percentage of contribution: 80 %   Date: 15 /10_ /2019 _

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Rachel Brand conceived of the idea for the manuscript, developed the intial draft and managed revisions.

Second Author

Name: Susan Rossell   Signature: Sh Rossell

Percentage of contribution: 5 %   Date: 15 / 10 / 2019

Brief description of your contribution to the 'paper':

Susan Rossell contributed to revisions of the draft manuscript.

Third Author

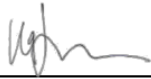Name: Sarah Bendall   Signature:

Percentage of contribution: 5 %   Date: 17 / 10 / 2019

Brief description of your contribution to the 'paper':

Sarah Bendall contributed to revisions of the draft manuscript.

Fourth Author

Name: Neil Thomas _____ Signature: _____
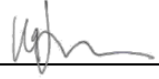
Percentage of contribution: 10 % Date: 15 / 10 / 2019

Brief description of your contribution to the 'paper':

  Neil Thomas contributed ideas to the first draft of the paper and contributed to revisions of the manuscript.

Principal Coordinating Supervisor:

Name: Neil Thomas _____ Signature: _____

Date: 15 / 10 / 2019

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

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DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Moment-to-Moment Associations Between Posttraumatic Stress Symptoms and Auditory Hallucinations in the Flow of Daily Life

First Author

Name Rachel Brand   Signature: _____

Percentage of contribution: 80 %   Date: 22/10/2019

Brief description of contribution to the 'paper' and your central responsibilities/role on project:
Rachel Brand conceived of the idea for the study, led on the development of the protocol, recruited participants, analysed data, and drafted the manuscript.

Second Author

Name: Sarah Bendall   Signature: _____

Percentage of contribution: 4 %   Date: 17 / 10 / 2019

Brief description of your contribution to the 'paper':
Sarah Bendall contributed to the design of the study and revisions of the draft manuscript.

Third Author

Name: Amy Hardy   Signature: _____

Percentage of contribution: 2 %   Date: 22 / 10 / 2019

Brief description of your contribution to the 'paper':
Amy Hardy contributed to revisions of the draft manuscript.

Fourth Author

Name: Susan Rossell _____   Signature: _Sh Rossell_____

Percentage of contribution: 2 %   Date: 15 / 10 / 2019

Brief description of your contribution to the 'paper':

Susan Rossell contributed to revisions of the draft manuscript.

Principal Coordinating Supervisor:

Name: Neil Thomas _____   Signature: _____

Date: 15 / 10 / 2019

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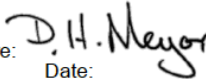
Authorship Indication Form

Fifth Author: Denny Meyer   Signature: D.H.Meyer
Percentage of contribution: __5.5__%   Date:
Brief description of contribution to the 'paper:
Denny Meyer provided support and supervision for the data analysis and contributed to revisions of the manuscript.

Sixth Author: Neil Thomas   Signature:
Percentage of contribution: __6.5__%   Date: 15/10/2019
Brief description of contribution to the 'paper:
Neil Thomas provided overall supervision, contributed to the design of the study and revisions of the manuscript.

Appendix V: Publication Three in published format

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DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

Do trauma-focused psychological interventions have an effect on psychotic symptoms? A systematic review and meta-analysis.

First Author

Name Rachel Brand   Signature: _____

Percentage of contribution: 80 %   Date: 15 / 10 / 2019

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Rachel Brand conceived of the idea for the manuscript, conducted the systematic review, quality assessments, and meta-analysis, and drafted the manuscript.

Second Author

Name: Carla McEnery   Signature: Carla McEnery

Percentage of contribution: 5 %   Date: __ / __ / ____

Brief description of your contribution to the 'paper':

Carla McEnery contirbuted to screening of articles and quality assessments of studies as well as commenting on the final manuscript.

Third Author

Name: Sarah Bendall   Signature: SBendgll

Percentage of contribution: 2.5 %   Date: 17 / 10 / 2019

Brief description of your contribution to the 'paper':

Sarah Bendall contributed to revisions of the draft manuscript.

Fourth Author

Name: Susan Rossell _____ Signature: _Sh Rossell_____

Percentage of contribution: 2.5 %   Date: 15 /10 / 2019

Brief description of your contribution to the 'paper': Susan Rossell contributed to revisions of the draft manuscript.

Fifth Author: Neil Thomas   Signature: _____
Percentage of contribution: 10 %   Date: 15/ 10/ 2019
Brief description of contribution to the 'paper:
Neil Thomas provided overall supervision, contributed to screening and quality assessments, gave advice on the analysis and contributed to revisions of the drafted manuscript.

Principal Coordinating Supervisor:

Name: Neil Thomas _____ Signature: _____

Date: 15 /10 / 2019

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

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DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

A Pilot Trial of Trauma-Focused Imaginal Exposure for Auditory Hallucinations.

First Author

Name Rachel Brand   Signature: _____
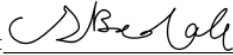
Percentage of contribution: 80 %   Date: 15/ 10/ 2019

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Rachel Brand conceived of the idea for the study, led on the development of the protocol, conducted data collection and analysis, was the trial therapist, and drafted the manuscript.

Second Author

Name: Sarah Bendall   Signature: _____

Percentage of contribution: 6 %   Date: 17 / 10 / 2019

Brief description of your contribution to the 'paper':

Sarah Bendall contributed to the design of the study and the study protocol, provided clinical supervision, and contributed to revisions to the draft manuscript.

Third Author

Name: Amy Hardy   Signature: _____

Percentage of contribution: 4 %   Date: 22 / 10 / 2019

Brief description of your contribution to the 'paper':

Amy Hardy provided clinical supervision and theoretical input to the write up of the manuscript.

Fourth Author

Name: Susan Rossell _____ Signature: _Sh Rossell_____

Percentage of contribution: 2.5 %   Date: 15 / 10 / 2019

Brief description of your contribution to the 'paper':

Susan Rossell contributed to revisions of the draft manuscript.

Principal Coordinating Supervisor:

Name: Neil Thomas _____ Signature: _____

Date: 15 / 10 / 2019

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

Authorship Indication Form

Fifth Author: Neil Thomas   Signature: _____
Percentage of contribution: __7.5__%   Date: 15/10/2019
Brief description of contribution to the 'paper:
Neil Thomas contributed to the design of the study and the protocol, provided overall supervision of the study and contributed to revisions of the draft manuscript.

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DECLARATION

We hereby declare our contribution to the publication of the 'paper' entitled:

A Tale of Two Outcomes: Remission and Exacerbation in the Use of Trauma-Focused Imaginal Exposure for Trauma-Related Voice-hearing. Key Learnings to Guide Future Practice.

First Author

Name Rachel Brand _____ Signature: _____

Percentage of contribution: __80_ %   Date: _15_ /10_ _2019_ _

Brief description of contribution to the 'paper' and your central responsibilities/role on project:

Rachel Brand conceived of the idea for the study, led the design and development of the protocol, was the study therapist, recruited participants, collected and analysed data and drafted the initial manuscript.

Second Author

Name: Amy Hardy _____ Signature: _____

Percentage of contribution: _7.5_ %   Date: _22/ 10 / 2019_

Brief description of your contribution to the 'paper':

Amy Hardy provided clinical supervision and provided theoretical input to the writing of the manuscript.

Third Author

Name: Sarah Bendall _____ Signature _____

Percentage of contribution: _5__ %   Date: _17_ 10 _2019

Brief description of your contribution to the 'paper':

Sarah Bendall contributed to the design of the study and protocol and to revisions of the draft manuscript.

Fourth Author

Name: Neil Thomas   Signature: _____

Percentage of contribution: 7.5 %   Date: 15 / 10 / 2019

Brief description of your contribution to the 'paper':

Neil Thomas provided overall supervision, contributed to the design of the study and development of the protocol and to revisions of the manuscript.

Principal Coordinating Supervisor:

Name: Neil Thomas   Signature: _____

Date: 15 / 10 / 2019

In the case of more than four authors please attach another sheet with the names, signatures and contribution of the authors.

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