Childhood trauma and language network function in the adult brain

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Chapter I: Lay summary

This project was interested in childhood trauma and auditory verbal hallucinations (AVH). AVH is a term used to mean hearing one or more voices in the absence of a person talking, that others cannot hear. People who have been diagnosed with a mental health problem such as Schizophrenia commonly hear voices, but some people without a mental health problem also hear voices. Hearing voices can be distressing and for this reason, researchers are interested in what causes people to hear voices, because this could lead to preventing people from developing voices or being able to offer better support and treatment to those who do. Childhood trauma means experiencing things in childhood that are potentially traumatic. For example, experiencing sexual, physical or emotional abuse, neglect, or experiencing events that another person is not responsible for, such as natural disaster or someone close to you dying. Some researchers have suggested that experiencing childhood trauma could lead people to become more vulnerable to hearing voices later in life.

This project had two main parts. The first part involved reviewing past research looking at the relationship between childhood trauma and hearing voices. The second part involved carrying out a new study.

The review of past research

As it had not been done before, a review was carried out to summarise the results of past studies that investigated the relationship between experiencing childhood trauma and hearing voices in adulthood in people with and without a mental health diagnosis. This was done by searching four online databases of published research studies and 682 studies were found. Then, these studies were screened using a detailed screening process to check whether the studies were relevant. 36 studies had used statistical analyses to investigate the relationship

between childhood trauma and hearing voices in adulthood and so were included within the review. These studies were published between 2003 and 2021 and were carried out in different countries in Europe, the Americas, Asia and Australia. The findings from the studies were summarised and an assessment of the quality of these 36 studies was completed using a well-known tool, with studies being given a rating of good, fair or poor. 31 of the studies found evidence that there is a relationship between childhood trauma and hearing voices in adulthood in both people with and without a mental health diagnosis. 5 studies did not find evidence of this, but most of these studies were poorer in quality, so the results may be less valid. Most types of childhood trauma, such as abuse, were found to have a relationship with hearing voices in adulthood. However, there was less evidence that neglect, and very little evidence that experiencing events that someone else was not responsible for are related to hearing voices in adulthood. Also, some studies found that other factors were involved in this relationship. The most common factor was dissociation, which is a feeling of being disconnected to yourself or the world, which sometimes happens when people experience traumatic events.

The new study

The study investigated how hearing voices might develop after experiencing trauma in childhood. Researchers have suggested that experiencing trauma in childhood while the brain is still developing may change the way that the brain develops and functions. This could make people more vulnerable to developing mental health problems in adulthood, including symptoms of psychosis such as hearing voices. Previous studies have found that adults who experienced childhood trauma tend to show altered function in certain areas of the brain that are linked to mental health problems. However, it is not clear what changes may happen in the brain following childhood trauma that could increase the risk of developing voices as no

other studies have investigated this. Functional Magnetic Resonance Imaging (fMRI) can be used to explore this, which takes pictures of the brain to detect which areas are active and connected to each other while participants are carrying out a task. This study analysed data from an fMRI study, which compared brain activity in a group of people who had experienced higher levels of childhood trauma with a group of people who had experienced lower childhood trauma while performing a task know to activate activity in the brain regions associated with hearing voices. People who had experienced higher levels of childhood trauma showed more activity in one area of their brain called the frontal operculum, than people who experienced lower levels of childhood trauma. However, this difference seemed to be explained by how much negative emotion they were feeling at the time of the fMRI scans. This area of the brain and another area of the brain called the supramarginal gyrus were also less connected to each other in people who experienced higher compared to lower levels of childhood trauma. These two areas of the brain have been found to be active when people hear voices. These results suggest that the brains of people who have experienced childhood trauma may function differently in areas that are associated with hearing voices, even when they do not have a mental health problem.

Conclusions

The results of both the review and the study may help people who hear voices and have experienced trauma in their childhood to better understand the reasons why they may have started to hear voices. Also, the results suggest that mental health services and other organisations like Health and Social care should be aware of the possibility that experiencing trauma in childhood can increase the risk of people hearing voices in adulthood. This could help them to become better at intervening and preventing people from developing voices. More research should be carried out to see if the same results from the study are found in

other groups of people. This could provide a better understanding of brain changes that may be responsible for increasing the risk of hearing voices following childhood trauma. Finally, more research could be conducted to investigate whether other treatments could be developed for people that hear voices. For example, treatments targeting the areas of the brain that function differently.

Chapter II: The relationship between childhood trauma and auditory verbal hallucinations in clinical and non-clinical adult samples: a systematic review

Abstract

Auditory verbal hallucinations (AVH) are a common symptom of psychosis and are experienced by those with various mental health diagnoses, but also within non-clinical populations. Childhood trauma increases the risk of developing psychosis and has been shown to be associated with positive symptoms of psychosis, with differential relationships between positive symptoms and childhood trauma subtypes found. However, the specific relationship between AVH and childhood trauma is unclear. Therefore, the current review aimed to, for the first time, summarise and synthesise research investigating this relationship within clinical and non-clinical populations. The review's questions were: 1) Is childhood trauma associated with AVH in adulthood? 2) Are any subtypes of childhood trauma more strongly associated with AVH? 3) Does the relationship exist in both clinical and non-clinical samples? 4) Do any other variables mediate the relationship? PsycINFO, PubMed, Web of Science and Scopus were searched, identifying 36 quantitative studies for inclusion in the review. Extensive support for the relationship between childhood trauma and AVH in clinical and non-clinical populations was found, with small to medium effect sizes. More tentatively, evidence of a combined or cumulative effect of childhood trauma on AVH was shown. There was also substantial evidence for the relationship between AVH and childhood abuse subtypes and interpersonal abuse, although predominantly within non-clinical samples with regard to physical abuse. There was weaker support for the relationship between neglect and AVH and little support for the relationship between non-victimisation events with AVH. Mediating factors were identified such as dissociation, provisionally supporting the theory that post-traumatic processes may be indicated in the relationship between childhood trauma

and AVH. The findings support the need for a trauma-informed approach in mental health services. However, further research including longitudinal designs is required to ascertain whether the relationship between childhood trauma and AVH is causal.

Introduction

Auditory verbal hallucinations (AVH) or "hearing voices" are commonly defined in the literature as the experience of hearing a voice or voices in the absence of external corresponding stimuli of which the subject feels they have little control over (Larøi et al., 2012). Auditory hallucinations are considered a positive symptom of psychosis along with delusions, and are a key feature of psychotic disorders (American Psychiatric Association, 2013). They are the most common type of hallucination experienced in psychotic disorders with an estimated, cross cultural, one year prevalence of 74% of people with a diagnosis of schizophrenia (Bauer et al., 2011). Although less prevalent, AVH are also experienced by other diagnostic groups, such as bipolar affective disorder (Toh et al., 2015) and borderline personality disorder (Kingdon et al., 2010), and within non-clinical populations, with around 5-15% of the general population reporting hearing voices (Beavan et al., 2011). This supports the continuum model of psychotic symptoms (Johns & Van Os, 2001; Larøi, 2012; Strauss, 1969) which proposes that AVH can range from subclinical or transient experiences in the general population to persistent clinical symptoms of psychosis. However, although AVHs are reported across the continuum, the experience of AVH in clinical and non-clinical populations has been found to differ. Clinical populations generally experience more frequent AVH with greater negative content and perceive voices as less controllable, more distressing, and have more negative beliefs about voices than in non-clinical voice hearers (Baumeister et al., 2017).

As the experience of AVH and other symptoms of psychosis such as paranoia (Freeman, 2007) are experienced across a spectrum of both clinical and non-clinical populations, research has moved away from focusing on groups of people that meet diagnostic categories such as schizophrenia, and toward investigating specific symptoms, or symptom-like experiences of psychosis in both clinical and non-clinical populations (Bentall, 2006; Van Os & Reininghaus, 2016). Importantly, this could generate a greater understanding of the etiological mechanisms related to specific symptoms of psychosis such as AVH. Childhood trauma has been extensively researched as a possible etiological factor in mental health disorders and is associated with a variety of mental health problems in adulthood, including anxiety, depression, psychosis and bipolar disorder (McKay et al., 2021). Childhood trauma as a construct is generally described as being exposed to potentially traumatic events before the age of 16 or 18 (Alameda et al., 2021). This includes physical, emotional and sexual abuse, physical and emotional neglect, bullying, household dysfunction and non-victimisation events such as natural disasters, illness and bereavement (Spalletta et al., 2020).

Extensive evidence suggests that experiencing traumatic events in childhood significantly increases the risk of developing psychosis (Matheson et al., 2013; Varese et al., 2012). Research investigating the prevalence rates of reported childhood trauma in clinical psychosis populations suggests that the estimated population attributable risk is 33% (Varese et al., 2012), indicating that childhood trauma is a substantial determinant of psychosis. Evidence for a dose-response effect has also been found, with a greater amount of childhood trauma exposures having a stronger relationship with symptoms of psychosis (Shevlin et al., 2007; Trauelsen et al., 2015). Cross-sectional and longitudinal designs have been used to investigate this relationship and although research of this nature cannot indicate a definite causal relationship (Bentall & Varese, 2012) it does suggest that childhood trauma is likely to

contribute to the development of psychosis symptomology. Childhood trauma has also been linked to increased severity of psychosis symptoms, such as hallucinations (Bailey et al., 2018) as well as reduced global functioning, slower improvement rates (Aas et al., 2016) and increased suicidal risk (Mohammadzadeh et al., 2019) within psychosis populations. This suggests that traumatic experiences in childhood not only increase the risk of developing psychosis but also increase the risk of developing more severe symptoms of psychosis with poorer outcomes.

Childhood trauma can be measured using a total cumulative score or by investigating specific subtypes of childhood trauma separately from each other. When investigating subtypes of childhood trauma in relation to specific symptoms of psychosis, differential effects have been found. Two recent systematic reviews and meta-analyses (Alameda et al., 2021; Bailey et al., 2018) have investigated the relationship between specific childhood trauma types and symptom dimensions in psychosis populations. They both found that positive symptoms of psychosis such as hallucinations and delusions are associated with childhood abuse in the form of sexual, physical and emotional abuse, and that childhood physical and emotional neglect are associated more with negative symptoms of psychosis. Bailey et al (2018), however, found a significant association between hallucinations (which included visual, auditory and olfactory hallucinations) and childhood neglect and sexual abuse. However, although they did not examine physical and emotional abuse, they concluded that all forms of childhood trauma are likely to be associated with hallucinations. These reviews did not analyse the specific relationship between AVH and childhood trauma, so it is unclear whether specific subtypes of childhood trauma have differential relationships with AVH. Indeed, within the literature, childhood sexual abuse is often reported as being particularly linked to AVH (McCarthy-Jones, 2011).

Many theories purporting to explain the mechanism of AVH following childhood trauma have been proposed. Although not globally accepted, a prominent theory posits that post-traumatic processes may be implicated in this relationship (Bentall et al., 2014; Steel, 2015; Steel et al., 2005). During traumatic experiences, it is thought that there is a shift in information processing style resulting in basic sensory, perceptual information being processed, rather than detailed contextual information, resulting in involuntary trauma memory intrusions (Ehlers & Clark, 2000). Dissociation sometimes occurs during the experience of a traumatic event, perhaps further reducing contextual processing, with people displaying higher schizotypy traits being more prone to dissociative states (Steel, 2015). It has been proposed that these decontextualised trauma memories could be appraised as external stimuli, perhaps due to failures in the ability to discriminate between internal and external perceptions or "source monitoring" (Bentall et al., 2014; Steel, 2015; Steel et al., 2005). These theories are supported by recent meta-analyses investigating psychological mediators in the relationship between childhood trauma and symptoms of psychosis, which both identified dissociation and post-traumatic stress disorder (PTSD) symptoms as mediators in this relationship (Bloomfield et al., 2021; Williams et al., 2018). Also supportive of these theories, thematic links between childhood trauma and the content of AVH have been found, such as the hallucinations reflecting similar content or themes as past traumatic experiences (Hardy et al., 2005) and hearing the voice of a past abuser (Corstens & Longden, 2013; Reiff et al., 2012).

Aims of the current review

Previous reviews have focused on investigating the relationship between childhood trauma subtypes and general positive symptoms or the broader category of hallucinations; none have

focused on examining the specific relationship between childhood trauma and AVH. Also, existing reviews have only focused on clinical/psychosis samples and have not taken into account non-clinical populations. As AVH are a highly prevalent symptom of psychosis, examining this specific relationship is important, as providing a greater understanding of the etiological factors of AVH and the specific mediating mechanisms of this relationship if found could have clinical implications for psychological intervention. To date, no systematic reviews have explored the specific relationship between childhood trauma and AVH in adulthood within clinical and non-clinical samples, indicating a gap in the literature. Therefore, the current review aimed to synthesise and critically evaluate the existing data relating to the association between childhood trauma and AVH in adulthood, to identify areas for further research and consider the clinical implications of the literature. Consequently, the main questions for the review were:

1. Is childhood trauma associated with AVH in adulthood?
2. Are any subtypes of childhood trauma more strongly associated with AVH?
3. Does the relationship exist in both clinical and non-clinical samples?
4. Do any other variables mediate the relationship?

Methodology

Search Strategy

The review was completed with reference to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (Page et al., 2021). The review was registered with PROSPERO on 02/07/2022 (registration number: CRD42021250722) and the search was conducted on 15th July 2021 using four databases: PsycINFO, PubMed, Web of

Science, Scopus. No restrictions were placed on publication date and the search was restricted to studies published in the English language.

Articles were identified using the following searches employing Boolean logic to identify key terms relating to childhood trauma and AVH: (“childhood trauma” OR “child maltreatment” OR “childhood advers*” OR “early life stress” OR "sexual abuse" OR "physical abuse" OR "emotional abuse" OR "neglect" OR "bullying") AND (“hallucinations” OR “auditory hallucinations” OR “auditory verbal hallucinations” OR “hear* voice*”)

Following the search, results were compiled, and duplicates were removed by use of EndNote referencing management tool and additional duplicates were removed manually. Studies were included in or excluded from the review based on the inclusion and exclusion criteria in two stages. Firstly, screening of the titles and abstracts was manually conducted by the author. Secondly, the full-texts were screened for eligibility by the author. Study authors were contacted to obtain the full-text if it was not available. A second reviewer independently screened 10% of studies (n = 68), and there were no disagreements about the exclusion or inclusion of studies in the systematic review (Cohen’s kappa = 1.00).

Inclusion and Exclusion Criteria

Inclusion criteria:

- Quantitative study design including cross-sectional, longitudinal and neuroimaging studies
- Participants 18 years of age or over
- Samples with a diagnosis of psychotic disorders (including a predominantly schizophrenia spectrum disorder sample; schizophrenia, psychosis not otherwise

specified, bipolar disorder with psychotic features, psychotic depression) and non-clinical populations

- Quantitative measure of AVH or auditory hallucinations [1]
- Quantitative measure of childhood trauma (before 18 years old) including physical, emotional and sexual abuse, physical and emotional neglect, bullying and other childhood adversity
- Peer-reviewed published articles
- Available in English language
- All geographical locations

Exclusion criteria:

- Qualitative designs, reviews, single case study designs, study protocols and book chapters
- Includes participants under the age of 18
- Samples consisting of or substantially including other diagnostic groups (for example; Bipolar Disorder, Post-Traumatic Stress Disorder, Borderline Personality Disorder)
- Includes participants who experience auditory hallucinations of an organic or drug-induced origin
- Includes only a measure of general hallucinations
- Includes only a measure of general lifetime trauma

[1] Studies were included that contained a measure of auditory hallucinations, which could include participants with non-verbal auditory hallucinations (hearing other sounds or noises). This decision was made as the most common reported auditory hallucination is verbal (American Psychiatric Association, 2013; Nayani & David, 1996), and often these terms are often used interchangeably to describe hearing voices. Also, some papers used the term auditory hallucinations to describe AVH and thus excluding these papers would have restricted the search.

- No statistical analysis of the relationship between childhood trauma and auditory hallucinations
- Grey literature, dissertations and publications without peer-review
- Unavailable in English language

Data Extraction

Included studies were examined in detail and characteristics from each study were extracted and recorded in a Microsoft Excel spreadsheet. This included:

- Authors, date of publication and location
- Study design
- Sample characteristics (including sample size, population, mean age and sex)
- Childhood trauma measure and childhood trauma type
- Auditory hallucination measure and auditory hallucination type
- Other key measures (for example, other psychological variables used in mediation analyses)
- Analyses
- Relevant statistical findings regarding the association between childhood trauma and AVH

Quality Assessment

The methodological quality of included studies was assessed by the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NHLBI, 2014). This tool is widely used in systematic reviews (for example; Gicas et al., 2022; Healy et al., 2019; Vila-Badia et al., 2021) and was chosen as the studies identified were cross-sectional or longitudinal in design. It consists of 14 questions

designed to assess the internal validity of studies for systematic review (see Appendix 1). The tool does not calculate a total summary score, but rather answers to individual items guide the reviewer to assess the risk of bias within each study based on any flaws found in the study design and execution. Based on this, a global quality rating of "Poor" (high risk of bias) "Fair" (some risk of bias) or "Good" (low risk of bias) was assigned to each study, based on a critical appraisal of the individual items in the context of each study. This approach is more widely recommended for systematic review of observational studies above quality assessment scales that provide a total score (Mueller et al., 2018). The quality of 10% (n = 4) of the included studies was assessed independently by a second reviewer. Any disagreements were resolved by discussion with the review team (Cohen's kappa = 0.80).

Data Synthesis

Due to the heterogeneous nature of included studies in terms of the types of childhood trauma measured and the analytical strategy, a narrative synthesis was deemed more appropriate than a meta-analysis (Siddaway et al., 2019) and was conducted in accordance with the PRISMA guidelines (Page et al., 2021). Effect sizes were extracted and/or calculated where possible to facilitate comparison between studies. Pearson's product moment correlation coefficient (r) and Spearman's rank correlation rho (r_s) were extracted and where chi square (χ^2) or tests of difference statistics were reported, results were transformed into a common standardised effect size (r) using online calculators (Lenhard & Lenhard, 2017). The interpretation of the magnitude of effect was based on Cohen's (1992) guidelines with values of 0.1, 0.3 and 0.5 and above indicating small, medium and large effects respectively. For studies using logistic regression, unstandardised Odds Ratios and 95% confidence intervals were extracted, which could not be standardised in the scope of this review due to the need for specialist software to compute standardised effect sizes. Effect sizes were not calculated for mediation analyses as

they are thought to have limited value (Hayes, 2018) and rather the indirect effect statistic was extracted.

Results

In total, 1243 studies were identified and following the removal of duplicates, 682 studies were screened. After screening of title and abstract, 486 articles were excluded that did not meet inclusion criteria. 196 full text papers were then screened resulting in 160 being excluded (reasons for exclusion outlined in Figure 1). 36 studies met inclusion criteria and were therefore included in the current review.

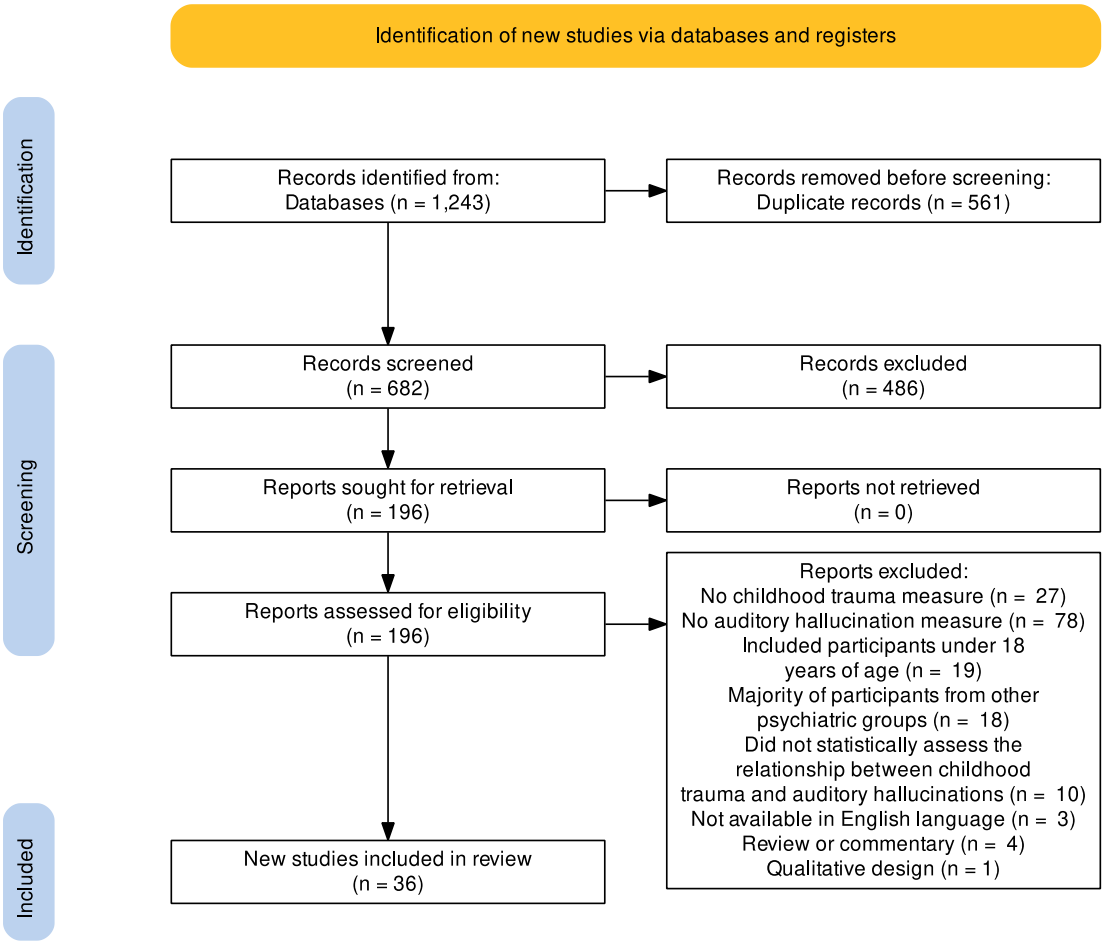

Figure 1.
PRISMA Flowchart Diagram of Study Selection. Generated using ShinyApp (Haddaway et al., 2021).

Study characteristics and design

Key characteristics and main findings of included studies alongside effect sizes are summarised in Table 1. The year of publication ranged from 2003-2021 and the 36 peer-reviewed studies were conducted in Argentina (*n* = 3), Australia (*n* =3), France (*n* = 2), India (*n* = 1), Netherlands (*n* = 4), Norway (*n* = 1), Poland (*n* = 1), South Korea (*n* = 1), Spain (*n* = 2), Turkey (*n* = 2), United Kingdom (*n* = 9), United States of America (*n* = 6) and across both Australia and the Netherlands (*n* = 1). 35 studies utilised a cross-sectional design, whilst only one employed a longitudinal cohort design, within which childhood trauma was measured prior to auditory hallucinations. In all studies, childhood trauma and auditory hallucinations were measured on one occasion with no repeated measures designs employed.

Table 1.

Summary of study characteristics and main findings

Authors (date), Country, Design (cross-sectional unless otherwise stated)	**Population, Sample size, Age (mean), gender (M:F:other), Sample characteristics**	**CT measure CT type**	**AH measure AH type**	**Other key measures**	**Analyses**	**Relevant Findings**
Abajobir et al (2017) **Australia** **Longitudinal**	NC 3752 20.6, NR Prospective prebirth cohort	Child protection records up to 14 years of age *CSA, CPA, CEA, childhood neglect*	YASR Presence of AH in last 6 months	-	Chi square, multivariate logistic regression	-Significantly higher rates of AH at 21-year follow-up in those who experienced any form of CT (test statistic not reported). -CEA (AOR= 1.83; [1.01–3.33] small effect) significantly associated with an increased risk of AH at 21-year follow-up. -Neglect (AOR = 2.14 [1.14–4.03] medium effect) significantly associated with an increased risk of AH at 21-year follow-up. -CEA (AOR = 1.98 [1.06–3.69] small effect) and neglect (AOR = 2.78 [1.37–5.68] medium effect) combined with one or more other CT subtypes significantly associated with AH at 21-year follow-up. -CPA and CSA not associated with AH.
Akbey et al (2019) **Turkey**	SCZ 100	CTQ	SAPS *Current AH severity*	-	Pearson Correlations	-Significant positive correlation between AH and CSA (r=0.206) -No significant correlations between AH and CT total score or any other CT subscales.

	38.7 69:31 Outpatients	*Total CT, all CTQ subscales.*				
Andrew et al (2008) **UK**	SSD and NC 43 (SSD: 22, NC: 21) SSD: 39.55, 13:9, NC: 50.67, 6:15 Recruited from mental health services and Spiritualist organisations.	PDS *Total CT and CSA*	PSYRATS, BAVQ-R *Beliefs about voices*	PDS, IES	Linear multiple regression	-CSA, number of lifetime traumatic events and current PTSD symptoms together predicted beliefs about voices (malevolence (66.4% of variance), benevolence (48.5% of variance) and omnipotence (42.5% of variance)). -CSA was not a significant predictor of beliefs about voices alone.
Begemann et al (2021) **Netherlands and Australia**	SSD and NC 413 (SDD= 166, NC with AVH=122, NC without AVH=125)	CTQ *Three clusters of CT emerged from a cluster analysis:* *-Low trauma (LT) (n=299; lower*	PSYRATS, BAVQ-R *AVH characteristics*	-	One-way ANOVA. Hierarchical cluster analysis. Clusters compared for differences in	SDD and NC with AVH groups, compared with NC without AVH reported significantly higher rates of: -CT overall -CSA -CEA -Graded significant differences found for CPA and CPN (SDD highest, NC without AVH lowest). (Unable to calculate)

	SDD: 38.65, 79:87. NC with AVH: 41.83, 37:85 NC without AVH: 42.88, 40: 85 Combination of two separate datasets: general population and inpatient and outpatients	*levels of all CTQ subtypes; relatively even distribution of groups)* *-Emotion-focused (EF) cluster (n=71; higher levels of CEA, CEN and CSA;* 49.30% NC with AVH, 35.21% SDD, 15.49% NC without AVH*)* *-Multi-trauma (MT) cluster (n=43; all CTQ subtypes except CEN;* 74.42% SSD, 23.26% NC with AVH, 2.33% NC without AVH).*)*	AVH characteristics using MANOVA.	-No differences in CEN. -MT cluster experienced AVHs as having a greater amount of negative content and rated voices more omnipotent compared to the LT cluster and reported less control over their AVHs compared to EF cluster -EF cluster started experiencing AVHs at a younger age compared to LT cluster -EF cluster rated voices as more benevolent compared to LT and MT clusters

Berg et al (2015)	PSY	CTQ	SCID-I	-	Spearman's correlations	Significant positive correlation between lifetime AVH and: -CPA (r_s=0.15) -CSA (r_s =0.13) -CPN (r_s =0.14) -CTQ total score (r_s =0.12)
Norway	454 NR, 249:205. Inpatients and outpatients	*Total CT, all CTQ subscales*	*Presence of Lifetime AVH*			Significant positive correlation between hearing one voice commenting and: -CPA (r_s =0.17) -CSA (r_s =0.13) -CPN (r_s =0.13) Significant positive correlation between hearing voices conversing and: -CTQ total score (r_s =0.192) -CPA (r_s =0.18) -CSA (r_s =0.16) -CEA (r_s =0.12) -CEN (r_s =0.14) -CPN (r_s =0.20)

Bortolon, Seillé and Raffard (2017) 425 **France** 36.23, 62:363 General population	NC 	CTQ *CTQ subscales* 	LSHS *AH Proneness* 	SQ-SF, DES 	Partial Least Squares Structural Equation Modelling with bootstrapping 	-CSA (b=0.036) had a significant indirect impact on AH proneness through maladaptive schemas (Subjugation, Vulnerability) and dissociation. -CEA (b=0.168) had a significant indirect impact on AH proneness through maladaptive schemas (Subjugation, Vulnerability, Abandonment) and dissociation. -CPA (b=0.108) had a significant indirect impact on AH proneness through dissociation alone.
Bortolon and Raffard (2018) 403 **France** 33.24, 72:331 General population	NC 	CTQ *Total CT* 	LSHS- AVH subscale *AVH Proneness* 	DES 	Partial Least Squares Structural Equation Modelling with bootstrapping 	-Defensive dissociation partially mediated the association between CT and AVH (b=0.124).
Connor and Birchwood (2012) 74 **England** 43, 44:30	SSD 	CTQ, s-EMBU *CTQ subscales, childhood dysfunctional* 	VPD, LEE (adapted for perceptions of voice-affiliation) 	- 	Pearson Correlations 	Significant positive correlation between CEA and: -voice power (r=0.37) -voice criticism (r=0.33). Emotional warmth from father negatively correlated with: -voices' emotional support (r = -0.25) -voices' criticism (r = -.29 $p < 0.05$)

	Outpatients	*affiliations (rejection, overprotection and warmth from parent)*	*AVH power and expressed emotion*			Rejection from parents positively correlated with voices' intrusion (r = .25 and r = 0.24)
Daalman et al (2012) **Netherlands**	NC and PSY 351 (PSY with AVH=100, NC with AVH=127, healthy controls=124) PSY: 38.02 44:66 NC: 42.41, 41:86 Controls: 43.06, 40:84 Outpatient and general population	CTQ *CTQ subtypes*	PSYRATS *AVH characteristics*	-	Chi Square, step-wise multinomial logistic regression, Spearman correlations	NC and PSY groups compared to controls had a greater chance of reporting: -CSA (OR=2.51 and OR=3.57 respectively) -CEA (OR=7.3 and OR=5.56 respectively) No CT subtypes were able to distinguish between positive or negative emotional valance of AVHs. No significant correlations found between CSA and CEA and AVH characteristics.
Freeman and Fowler (2009)	NC 200	LSC	CAPS (AVH scale)	-	Chi square	Significant association with lifetime AVH and: -CT total (r=0.16) -Childhood rape (r=0.30)

UK 37.5, 100:100 General population		*Total CT, CSA, childhood rape, CPA*	*Lifetime AVH*			-CPA (r=0.15)
Gomez, Kaehler and Freyd (2014) 566 **USA** 19.96, 215:351 Students	NC	BBTS- adapted- 2 CSA questions *CSA*	CIDI - Beliefs and experiences module *Lifetime AH*	-	Multiple logistic regression	Medium betrayal, but not high betrayal CSA significantly predicted AH (OR not reported)
Galletti et al (2017) **USA** 247 23.9, 184:63 Inpatients	FEP	CTQ, TEC, PN, PHD, VE, FDB, SCS (used a previous factor analysis to define three factors of CT) *Environmental Violence,*	SAPS *Current AH severity*	-	Spearman correlation	Significant positive correlation between AH and: -Interpersonal abuse (r_s=0.21) -Environmental violence (r_s=0.25), but not neglect.

		Interpersonal abuse, Neglect				
Goldstone, Farhall and Ong 2012) **Australia**	NC and PSY 233 (NC=133, PSY=100) NC: NR, 55:78 PSY: NR, 56:54 Outpatients and general population/students	ETI-SR (CSA questions adapted to be less distressing) *CSA, CEA and CPA*	LSHS *AH proneness*	SRLE, MCQ	Pearson correlation, path analyses	In NC sample: Significant positive correlations between AH and: -CEA (r=0.30) -CPA (r=0.20) -No association between AH and CSA -CEA combined with life hassles mediated by cognitive confidence and experiential avoidance predicted 20% of variance in the predisposition to AH. In PSY sample: -Significant positive correlation between CSA and AH (r=0.25) -No association between AH and CPA or CEA -CSA combined with life hassles partially mediated by cognitive confidence and experiential avoidance predicted 11% of variance in the predisposition to AH.
Hardy et al (2016) **UK**	PSY (relapsing) 228	THQ	SAPS	SRS-PTSD	Chi Square, mediation analyses using linear regression	-Significant association between CSA and the presence of AH (r=0.17) -No association between AH severity and CPA, CEA or non-victimisation events.

	38.24, 165:63 Inpatients and outpatients	*CSA, CPA, CEA, non-victimisation events in childhood*	*Current AH severity*			-No association between combined/cumulative CT on AH. -Relationship between CSA and AH mediated by post-traumatic avoiding and numbing (OR=1.48) and hyperarousal (OR=1.44), but not intrusive trauma memory or negative other beliefs.
Kim, Kim and Kim (2018) **South Korea**	SSD 42 32.6. 22:20 Inpatients	CTQ *Total CT, all CTQ subscales*	SAPS *Current AH severity*	-	Kendall correlation coefficient	No association between AH with CT total or any subtypes.
Mason et al (2009) **UK**	PSY with delusional component 39 NR, 23:16 Mental health services	CTQ *CPA, CSA, CEA*	SCAN-2.1 *Presence of current AH*	-	Logistic regression	AH were not significantly predicted by CPA, CSA or CEA.
Misiak et al 2016)	FEP	ETI-SR	OPCRIT	-	Mann Whitney U, Fishers Test,	In participants who had experienced CT, compared to those who had not:

Poland	94 54 (24.81): 40 (28.62) Inpatients	*General trauma (range of non-victimisation events/ witnessing violence/bereavement),CT total, CPA, CSA, CEA*	*Lifetime AVH (5 types)*		Spearman correlation, Linear regression	-The number of lifetime AVH types were significantly higher (unable to calculate) -Third person AVHs were significantly more frequent (r=0.26) -abusive/accusatory/persecutory AVHs were significantly more frequent (r=0.41) No differences in frequency of running commentary voices between groups. -Significant positive correlation between number of lifetime AVH types experienced and: -Total CT (r_s=0.21, not significant when genders analysed separately) -CSA (r_s=0.24- females only r_s=0.41, not significant in males) -General trauma (r_s=0.20, not significant when genders analysed separately) No correlation between lifetime AVH types and CPA or CEA. -CSA predicted lifetime number of AVH types only in females.
Offen, Waller and Thomas (2003) **UK**	SSD with AVH 26	One CSA question *CSA*	BAVQ *Beliefs about AVH*	-	Mann Whitney U, Spearman correlation	-No difference in BAVQ subscales between those who had and had not experienced CSA. -Significant negative correlation between age at first CSA and beliefs that voices are malevolent (r_s=-0.67), but no other BAVQ subscales.

	34, 19:7 Outpatients					
Pearce et al (2017) **UK**	SSD 112 40.26, 81:30:1 Online recruitment of those with lifetime SSD diagnosis/treatment	BBTS *Childhood Interpersonal Trauma (CIT)*	CAPE (AVH subscale) *AVH frequency*	DES, RQ	Spearman correlation, mediation analyses (Hayes (2013) PROCESS method with bootstrapping)	-Significant positive correlation between CIT and AVH (r_s=0.26). -Dissociation (not fearful attachment) mediated relationship between CIT and AVH (b=0.09).
Perona-Garcelan et al (2010) **Spain**	SSD 37 36.46, 31:6 Outpatients	TQ *Total CT*	PANSS items (unspecified) *Current AH*	-	Mann Whitney U	Participants with AH reported a significantly higher number of CT experiences than those who did not report AH (unable to calculate).

Perona-Garcelan et al (2012) **Spain**	SSD 71 39.08, 54:17 Outpatients	TQ *Total CT*	PANSS items (unspecified) *Current AH*	DES	Correlations (test NR). Simple and multiple mediation analyses (Preacher and Hayes (2004 and 2008 respectively) method with bootstrapping).	-Significant positive correlation between CT and AH (r=0.36). -In simple mediation analyses, dissociation significantly mediated this relationship (b=0.21). -In multiple mediation analyses, only depersonalisation mediated this relationship (b=0.19).
Pilton et al (2016) **UK**	PSY (voice hearers) 55 42.16, 44:11 Mental health trusts and voluntary services	CTQ *CTQ subscales*	PSYRATS-AH, BAVQ, VAY *AH severity in past week* *AVH characteristics*	PAM	Mediation analyses (Preacher and Hayes (2004) method with bootstrapping).	-Anxious attachment mediated the relationship between AVH severity and: -CSA (b=0.14) -CEA (b=0.14) -CPN (b=.16)

Prokopez et al (2018) **Argentina**	SCZ (female sample) 50 52.80, 0:50 Inpatients and outpatients	ACE *Total CT*	One novel question *Lifetime AH*	-	Chi Square	Participants reporting 4 or more ACEs were more likely to have experienced lifetime AH that those reporting 0-3 ACE (r=0.30)
Prokopez et al (2020) **Argentina**	SCZ 100 45.82, 50:50 Mental health services	ACE *Number of ACEs including abuse, neglect and household dysfunction*	PSYRATS *AH severity*	-	Spearman correlation,	-Significant positive correlation between number of ACE and severity of AH (r_s=0.23). -Significantly more severe AH in those who experienced >5 ACE compared to those who experienced 0-4 ACE (unable to calculate).
Rajkumar (2015) **India**	SCZ 62 35.3, 31:31	CTQ *Total CT, all CTQ subscales*	PANSS *Presence of AH*	-	Independent t-tests	No significant difference in any CTQ scores between participants who experienced AH and those who did not.

	Outpatients					
Rosen et al (2018) **USA**	SSD 61 47.98, 28:33 Outpatients	ACE *Number of ACE including abuse, neglect and household dysfunction*	PSYRATS *AVH severity and characteristics*	-	Pearson's correlations	Significant positive correlations between number of ACE and: -AVH severity (r=0.43) -AVH frequency (r=0.28) -Negative AVH content (r=0.44) -AVH distress (r=0.38) -AVH controllability (r=0.26)
Rosen et al (2020) **USA**	SSD 78 46.69, 40:38 Mental health services	ACE *Number of ACEs including abuse, neglect and household dysfunction*	PSYRATS *AVH severity*	VISQ	Mediation analyses (Hayes (2007) PROCESS method with bootstrapping).	Dialogic inner speech mediated the association between AVH severity and: -Total CT (0.53) -Childhood abuse (0.89) -Household dysfunction (1.04) Neglect was not associated with AVH
Shah et al (2014) **Australia**	PSY 1825	Novel instrument (interview)-national framework	DIP	-	Univariate logistic regression,	-Participants reporting CT were more significantly more likely to report lifetime AH (OR=1.30 [1.0-1.6]).

	38.4, 851:416 Psychosis sample from general population survey	definitions of child abuse. *Presence of CT (CSA, CPA, CEA, neglect)*	*Lifetime AH*		multiple logistic regression.	-AH was not a significant predictor of CT in multiple regression analyse with other clinical profile variables.
Sheffield et al (2013) **USA**	SSD 114 37.3, 58:56 Inpatient and outpatient	CTQ *Total CT and all subtypes*	SCID *Presence of lifetime AH*	-	MANOVA, One-way ANOVA, binary logistic regression	AH did not predict any subtypes of CT when all were entered into a MANOVA. -Compared with controls, participants reporting lifetime AH reported significantly more CSA, CPA and CEA (unable to calculate). Only CSA remained significant when controlling for depression. -CSA, CPA and CEA together predicted AH in logistic regression. Post-hoc analyses with a subgroup of participants who experienced CPA and CEA without CSA found no significant differences in abuse levels between those who had and had not experienced AH.
Shevlin et al (2011) **USA**	NC 2353	CIDI (3 items from PTSD module)	CIDI (1 item from Psychosis module)	-	Chi square, multivariate	Lifetime AVH significantly associated with: -CPA (r=0.13) -CSA (r=0.09)

					binary logistic regression	-Childhood rape (r=0.14) -Participants who reported childhood rape were 3.5 times more likely to report AVH than those that had not. -CPA (OR=4.55, [1.96-10.57]) and rape in childhood (OR=2.97, [1.39-6.33]), but not other CSA, increased the probability of experiencing AVH. -A significant dose-response relationship was found with those who experienced two (OR=5.39 [1.91-15.21]) and all three (OR=11.01 [3.59-33.74]) types of abuse more likely to report AVH compared to participants with no CT history.
	44.35, 988:1365 General population	*CPA, CSA (excluding rape), childhood rape*	*Lifetime AVH*			
So et al (2016) **Netherlands**	PSY and NC 301 (PSY with AVH=40, NC with AVH=135, healthy controls=126)	CTQ *Total CT, all CTQ subscales*	PSYRATS, BAVQ *AVH beliefs and characteristics*	-	MANOVA with follow up ANOVA	-AVH groups reported significantly higher CT on all subscales than controls (unable to calculate) -PSY reported significantly higher CPA and total CT than NC with AVH (unable to calculate) CSA did not predict any responses to voices

	PSY=45.43, 8:32, NC=50.60, 43:92, Controls=50.80, 40:86 Mental health services and general population					
Sommer et al (2010) **Netherlands**	NC 163 (with AVH=103 (94 used in CT analyses), without AVH=60) With AVH= 44, 30:73, Without AVH=46, 18:42 General population	CTQ *Total CT, all CTQ subscales*	PSYRATS, LSHS *Presence of AVH*	-	t-tests, multivariate GLMs (test NR), logistic regression	Participants experiencing AVH reported significantly more: -Total CT (r=0.39) -CPA (unable to calculate) -CSA (unable to calculate) -CEA (unable to calculate) -CEN (unable to calculate) -No significant difference in CPN between the groups. -Total CT did not significantly predict AVH in logistic regression analysis (with schizotypal personality and family history variables).
Sporle, Winter and Rhodes (2011)	PSY	CTQ (CSA subscale)	PSYRATS	-	Mann Whitney-U	No significant difference in AH between CSA and non-CSA groups.

UK	21 (CSA group=10, non-CSA group=11) 40.9, 10:11 Psychiatric services	*CSA*	*Current AH*			
Üçok and Bıkmaz (2007) **Turkey**	FEP 57 NR, 29:28 Inpatients	CAQ, CTQ (administered via interview when participants in remission) *Total CT, all CTQ subscales.*	SAPS *Current AH severity*	-	Mann-Whitney U, Spearman's correlations	-Significant positive correlation between CT total and AH (r_s=0.27). -Significantly higher AH and voices commenting in those who reported CEA compared to those who did not (unable to calculate). -No differences in AH severity in those who reported CPA, CSA, CPN or CEN compared to those who did not.
Vallejos et al (2017) **Argentina**	SCZ (male sample) 51 41.27, 51:0	ACE *Number of ACEs including abuse, neglect and*	One novel question *Lifetime AH*	-	Chi square	Significant association between number of ACEs experienced and lifetime AH (r=0.34).

	Inpatients and outpatients	*household dysfunction*				
van Nierop et al (2014)	NC	NEMISIS	CIDI (Psychosis add on), additionally SCID-I for subgroup only	-	Logistic regression	Lifetime AVH was significantly associated with: -CT total (OR=1.42 [1.30-1.55]) -CEN (OR=1.38, [1.25-1.53]) -CEA (OR=1.34 [1.22-1.48]) -CPA (OR=1.25, [1.16-1.36]) -CSA (OR=1.28, [1.20-1.38]). Growing up in foster care and bereavement did not meet the significance level set ($p<0.001$). In sensitivity analyses in a subgroup of participants (n = 384) in which psychotic symptoms were validated by interview, only CSA was confirmed as a significant association with AVH (OR=1.26, [1.10-1.44]).
	13722					
Netherlands		*CT total, CEN, CPA, CEA, CSA, bereavement and being fostered*				
	42.6, 6274:7447					
	General population		*Lifetime AVH*			

Note. NR=Not reported; NC=Non-Clinical; SCZ=Schizophrenia; FEP=First-episode Psychosis; PSY=Psychosis; SSD=Schizophrenia Spectrum Disorder; AH=Auditory Hallucinations; AVH=Auditory Verbal Hallucinations; CT=Childhood Trauma; CSA=Childhood Sexual Abuse; CPA=Childhood Physical Abuse; CEA=Childhood Emotional Abuse; CPN=Childhood Physical Neglect; CEN=Childhood Emotional Neglect; PTSD=Post-Traumatic Stress Disorder.

Key. CTQ=Childhood Trauma Questionnaire (Bernstein et al., 2003); PDS=Post-Traumatic Diagnostic Scale (Foa et al., 1997); s-EMBU=Egna Minnen Betraffance Uppfostrab – "My memories of upbringing"(Arrindell & Engebretsen, 2000); LSC=Life Stressor Checklist (McHugo et al., 2005); BBTS=Brief Betrayal Trauma Survey (Goldberg & Freyd, 2006); TEC=Trauma Experiences Checklist (Cristofaro et al., 2013); PN=Parental Nurturance (Barnes & Windle, 1987); PHD=Parental Harsh Discipline (Ge et al., 1994); VE=Violence Exposure (Mrug et al., 2008); FDB=Friends' Delinquent Behaviour (Mrug et al., 2012); SCS=School Connectedness Scale (Sieving et al., 2001); ETI-SR=Early Trauma Inventory-Self Report (Bremner et al., 2007); THQ=The Trauma History Questionnaire (Stamm, 1996); TQ=Trauma Questionnaire (Davidson & Smith, 1990); ACE=Adverse Childhood Experiences Questionnaire (Felitti et al., 2019); CIDI=The Composite International Diagnostic Interview (Kessler & Üstün, 2004); CAQ=Childhood Adversity Questionnaire; (Sar et al., 1999), NEMISIS=Netherlands Mental Health Survey and Incidence Study (Bijl et al., 1998); YASR=Young Adult Self-report checklist (Achenbach, 1997); SAPS=The Scales for the Assessment of Positive Symptoms (Andreasen, 1984); PSYRATS=Psychotic Symptom Rating Scales (Haddock et al., 1999); BAVQ= Beliefs About Voices Questionnaire (Chadwick et al., 2000); LSHS=Launay-Slade Hallucinations Scale (Launay & Slade, 1981); VPD=Voice Power Differential Scale (Birchwood et al., 2000); LEE=Level of Expressed Emotion Scale (Cole & Kazarian, 1988); CAPS=Cardiff Anomalous Perceptions Scale (Bell et al., 2006); SCAN=Schedules for Clinical Assessments in Neuropsychiatry (Wing et al., 1990); OPCRIT=Operational Criteria for Psychotic Illness Checklist (McGuffin et al., 1991); CAPE=Community Assessment of Psychotic Experiences (Schlier et al., 2015); PANSS=Positive and Negative Syndrome Scale (Kay et al., 1967); VAY=The Voice and You (Hayward et al., 2008); DIP=Diagnostic Interview for Psychosis (Castle et al., 2006); SCID-I=Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Spitzer et al., 1992); IES=Impact of Events Scale (Horowitz et al., 1979); SQ-SF=The young schema questionnaire short form (Young, 2005); DES=Dissociative experiences scale (Darves-Bornoz et al., 1999); SRLE=Survey of recent life experiences (Kohn & Macdonald, 1992); MCQ=Metacognitions questionnaire (Wells & Cartwright-Hatton, 2004); SRS-PTSD=Self-report Scale for Post-traumatic Stress Disorder (Carlier et al., 1998); RQ=Relationship Questionnaire (Bartholomew & Horowitz, 1991); PAM=Psychosis Attachment Measure (Berry et al., 2008); VISQ=Varieties of Inner Speech Questionnaire (McCarthy-Jones & Fernyhough, 2011).

Sample characteristics

Sample sizes ranged from *n* = 21 (Sporle et al., 2011) to *n* = 13,722 (Van Nierop et al., 2014) with a median sample size of 106 participants. In fourteen studies the majority of participants identified as male, whilst in nine studies the majority of participants identified as female, with one study recruiting a female-only sample (Prokopez et al., 2018) and another recruiting a male-only sample (Vallejos et al., 2017). Of the remaining studies, twelve recruited a more balanced gender sample and one study did not report the gender of participants (Abajobir et al., 2017). The mean age of study participants ranged from 19.96 years (Gómez et al., 2014) to 52.80 years (Prokopez et al., 2018) and three studies did not report the mean age of participants (Goldstone et al., 2012; Mason et al., 2009; Üçok & Bikmaz, 2007).

Five studies used both clinical and non-clinical samples, eight studies used purely nonclinical samples and twenty-three used purely clinical samples (for example, schizophrenia spectrum disorder, first episode psychosis). Non-clinical samples were recruited from the general population (*n* = 7), student populations (*n* = 1), a prospective prebirth cohort (*n* = 1) and spiritualist organisations (*n* = 1) and three studies utilised data from general population surveys. Clinical samples were recruited from inpatient facilities (*n* = 4), outpatient facilities (*n* = 7), inpatient and outpatient facilities (*n* = 8) and mental health facilities that did not specify the type of service participants were recruited from (*n* = 7). In addition, one study recruited self-selected participants via an online survey who self-reported having a schizophrenia spectrum diagnosis and/or having received psychological or psychopharmacological treatment for experiences related to psychosis (Pearce et al., 2017) and one study used a randomly selected psychosis sample from a general population survey stratified by age (Shah et al., 2014).

Childhood trauma measures

A variety of measures were used to assess childhood trauma. The majority of studies used retrospective self-report questionnaires (n=31) and interviewer rated measures (n=4) with the exception of one study (Abajobir et al., 2017), which utilised child protection records up to 14 years of age as a prospective substantiated measure of childhood trauma.

The most frequently used questionnaire was the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003) which measures five types of childhood trauma (sexual, physical and emotional abuse and physical and emotional neglect) occurring before 18 years of age. 13 studies used the CTQ and a further three studies used the CTQ alongside other questionnaires. Among these studies, most utilised total childhood trauma scores and/or all five subtypes of the CTQ. One study (Begemann et al., 2021) conducted a cluster analysis from which three childhood trauma groups emerged and were compared in analyses. Another study (Galletti et al., 2017) used the CTQ alongside other childhood trauma measures to create three factors of childhood trauma: Environmental Violence, Interpersonal Abuse and Neglect. Five studies used the Adverse Childhood Experiences (ACE) questionnaire (Felitti et al., 2019), which provides a total count of the number of traumatic childhood experiences (abuse, neglect and household dysfunction) before 18 years of age.

Other lesser used retrospective self-report questionnaires were used to measure a variety of childhood trauma subtypes (e.g. abuse, neglect, non-victimisation events) which included checklist based questionnaires such as the Life Stressor Checklist (McHugo et al., 2005) and the Early Trauma Inventory Self-Report (Bremner et al., 2007). In addition, one study (Pearce et al., 2017) used the Brief Betrayal Trauma Survey (BBTS; Goldberg & Freyd, 2006) to measure childhood interpersonal abuse.

Three studies utilising national survey data (Shah et al., 2014; Shevlin et al., 2011; Van Nierop et al., 2014) used interviewer rated measures of childhood trauma, such as the Composite International Diagnostic Interview (CIDI; Kessler & Üstün, 2004). In addition, three studies measured only childhood sexual abuse, of which one study used the CTQ sexual abuse subscale (Sporle et al., 2011). Another (Gómez et al., 2014) used modified sexual abuse questions from the BBTS, to assess childhood sexual abuse up to 13 years of age and the third (Offen et al., 2003) measured childhood trauma using a single novel question about experiencing CSA, which was taken into consideration as a methodological weakness when assessing the quality of this study.

Auditory hallucination measures

The majority of studies used structured interviewer rated measures (n = 22) to assess for auditory hallucinations/AVH, whilst seven studies used self-report questionnaires only and five used a combination. A further two studies used a single novel question to measure the experience of lifetime auditory hallucinations (Prokopez et al., 2018; Vallejos et al., 2017), which was taken into consideration when conducting the quality assessment.

Interviewer-rated measures included the Scales for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), which measures the severity of current auditory hallucinations and which five studies used. Another five studies used the auditory hallucination subscale of the Psychotic Symptoms Rating Scale (PSYRATS; Haddock et al., 1999) which measures the severity as well as characteristics of AVH (for example, frequency, controllability, negative content and beliefs about the origin of voices). A further five studies used the PSYRATS alongside self-report questionnaires. Some studies utilised items from interviewer rated checklists and scales measuring symptoms of psychosis, such as the CIDI and the Positive

and Negative Syndrome Scale (PANSS; Kay et al., 1967) to measure the presence or severity of current or lifetime auditory hallucinations.

Self-report questionnaires included surveys assessing the presence of lifetime (Cardiff Anomalous Perceptions Scale; Bell et al., 2006) and frequency of current AVH (Community Assessment of Psychotic Experiences; Schlier et al., 2015). Questionnaires measuring cognitive, behavioural and affective responses to AVH were also employed. For example, the Beliefs About Voices Questionnaire (BAVQ; Chadwick et al., 2000) was used in five studies, which assesses beliefs about and behavioural and emotional responses to AVH (voices' perceived malevolence, benevolence and omnipotence as well as resistance to and engagement with voices). Three studies recruiting non-clinical samples and one recruiting a mixed sample used the Launay-Slade Hallucination Scale (LSHS; Launay & Slade, 1981), which is designed to measure auditory hallucination proneness in non-clinical populations. Some studies (n = 16) coded AVH as present or absent, which was then used in statistical tests such as Chi Square tests, Logistic Regression, or to create groups for independent t-tests.

Other measures

Eight studies that carried out mediation analyses used measures to assess for other psychological variables. All used self-report questionnaires, which included the Dissociative Experiences Scale (DES; Darves-Bornoz et al., 1999) as a measure of dissociation and which four studies used. Measures of PTSD symptoms were used such as the Self-report Scale for PTSD (SRS-PTSD; Kohn & Macdonald, 1992) and the Post-traumatic Diagnostic Scale (PDS; Foa et al., 1997). In addition, types of inner speech were measured by the Varieties of Inner Speech Questionnaire (VISQ; McCarthy-Jones & Fernyhough, 2011), schemas and metacognitions were measured by the Young Schema Questionnaire Short form (SQ-SF;

Young, 2005) and the Metacognitions questionnaire (MCQ ; Wells & Cartwright-Hatton, 2004) respectively and attachment was measured by the Relationship Questionnaire (RQ; Bartholomew & Horowitz, 1991) and the Psychosis Attachment Measure (PAM; Berry et al., 2008).

Quality assessment of included studies

Quality assessment ratings can be found in Table 2. Twenty-two studies received global ratings of "Fair", six received global ratings of "Good" and eight received global ratings of "Poor". A main limitation was the lack of controlling for confounders, with half (n = 18) of included studies controlling for confounders, such as demographic information including age and gender, whilst half did not (n = 18). Also, most studies (n = 32) did not provide a sample size justification or power description or provide estimates of variance and effect size. No studies reported whether assessors were blinded to exposure status of participants and most (n = 27) did not report the participation rate of eligible persons. Areas of strength included clearly stated and defined research questions or objectives and study population, and the use of reliable and valid measures employed for both childhood trauma and auditory hallucinations in the majority of studies. Unusually, although most of the included studies were cross-sectional in design and childhood trauma was measured retrospectively, there was sufficient timeframe between exposure (childhood trauma) and outcome (AVH in adulthood) to see an effect between the two variables.

Table 2.

Quality assessment of studies

Authors and date	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***11***	***12***	***13***	***14***	***Global Rating***
Abajobir et al (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NR	No	Yes	Good
Akbey et al (2019)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Andrew et al (2008)	Yes	Yes	NR	No	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Poor
Begemann et al (2021)	Yes	Yes	NR	No	Yes	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Berg et al (2015)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Bortolon et al (2017)	Yes	Yes	NR	Yes	Yes	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Good
Bortolon and Raffard (2018)	Yes	Yes	NR	Yes	Yes	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Good
Connor and Birchwood (2012)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Daalman et al (2012)	Yes	Yes	NR	No	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Freeman and Fowler (2009)	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	No	Yes	NR	NA	Yes	Fair
Gomez et al (2014)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Galletti et al (2017)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Goldstone et al (2012)	Yes	Yes	NR	No	No	No	Yes	Yes	No	No	Yes	NR	NA	No	Fair
Hardy et al (2016)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Kim et al (2018)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Mason et al (2009)	No	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Poor
Misiak et al I2016)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Good

Offen et al (2003)	Yes	Yes	Yes	Yes	No	No	Yes	No	No	No	Yes	NR	NA	No	Poor
Pearce et al (2017)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Perona-Garcelan et al (2010)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	CD	NR	NA	No	Poor
Perona-Garcelan et al (2012)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	CD	NR	NA	Yes	Fair
Pilton et al (2016)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Prokopez et al (2018)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	No	NR	NA	No	Poor
Prokopez et al (2020)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Rajkumar (2015)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	CD	NR	NA	No	Poor
Rosen et al (2018)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Rosen et al (2020)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Shah et al (2014)	Yes	Yes	NR	Yes	No	No	Yes	No	No	No	Yes	NR	NA	Yes	Fair
Sheffield et al (2013)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Shevlin et al (2011)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
So et al (2016)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Sommer et al (2014)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Good
Sporle et al (2011)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Poor
Üçok and Bıkmaz (2007)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	Yes	NR	NA	No	Fair
Vallejos et al (2017)	Yes	Yes	NR	Yes	No	No	Yes	Yes	Yes	No	No	NR	NA	No	Poor
van Nierop et al (2014)	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes	NR	NA	Yes	Good

Note: 1=clear research question/objective, 2=clearly defined study population, 3=participation rate >50%, 4= Participants recruited from same populations, uniform inclusion/exclusion criteria, 5=sample size justification, 6=exposures measures prior to outcome, 7=sufficient timeframe to see association, 8=different levels of exposure measures, 9=valid/reliable exposure measures, 10=exposure assessed more than once, 11=valid/reliable outcome measures, 12=assessors blinded to exposure status, 13=loss to follow-up <20%, 14=confounding variables taken into account (See Appendix 1 for full questions)
NA=not applicable, NR=not reported, CD=cannot determine

Main findings

Is childhood trauma associated with AVH in adulthood?

Overall, most studies found evidence of a relationship between childhood trauma and AVH (*n* = 31) in total childhood trauma scores and/or at least one type of childhood trauma. Five studies – all of which recruited clinical samples – did not find any evidence of a relationship between childhood trauma and auditory hallucinations (Kim et al., 2018; Mason et al., 2009; Offen et al., 2003; Rajkumar, 2015; Sporle et al., 2011). Four of these studies were of poorer quality, with the exception of Kim et al (2018), which was given a quality rating of "Fair", and all had notably smaller sample sizes.

Twenty-one studies investigated the association between total scores of childhood trauma measures and AVH. Fifteen found a significant association as defined by a statistical significance threshold of $p<0.05$, with effect sizes ranging from small ($r_s=0.12$) to medium ($r=0.43$). Three did not find a significant association and a further three found mixed results, with some analyses finding a significant association and some analyses not finding a significant association within the same paper. Eighteen were assessed as being Fair or Good in quality, and three were assessed to be of Poor quality, one of which did not find a significant association.

Correlations and associations

In the longitudinal study (Abajobir et al., 2017) of higher quality, significantly higher rates of auditory hallucinations at 21-year follow-up were found in those who had experienced substantiated childhood trauma compared to those who had not. Significant positive correlations were found between childhood trauma total scores and current auditory hallucination/AVH severity (Perona-Garcelán et al., 2012; Prokopez et al., 2020; Rosen et al.,

2018; Üçok & Bikmaz, 2007) and between lifetime AVH and hearing voices conversing (Berg et al., 2015). Significant associations were found between childhood trauma and lifetime auditory hallucinations and AVH (Freeman & Fowler, 2009; Vallejos et al., 2017). One study also found positive correlations between total childhood trauma and lifetime auditory hallucination types, although not when genders were analysed separately (Misiak et al., 2016). In addition, significant positive correlations were found between childhood trauma total scores and voice characteristics such as frequency, distress, controllability and negative content (Rosen et al., 2018). Two studies (Akbey et al., 2019; Kim et al., 2018) did not find significant relationships between childhood trauma total scores and auditory hallucination severity.

Group differences

Significantly higher rates of total childhood trauma scores were found in four studies in clinical and non-clinical participants who experienced AVH compared to healthy controls (Begemann et al., 2021; So et al., 2016), in clinical participants who experienced auditory hallucinations compared to those who did not (Perona-Garcelán et al., 2010) and in non-clinical participants who experienced AVH compared to those who did not (Sommer et al., 2010). Significantly higher rates of lifetime, third person and abusive/accusatory/persecutory AVH were found in participants who reported childhood trauma compared to those who did not (Misiak et al., 2016). One study (Rajkumar, 2015) which was given a quality rating of "Poor" found no difference in childhood trauma levels in those who experienced auditory hallucinations to those who did not.

Logistic regression

Mixed results were found when logistic regression analyses were conducted, with significant associations found between childhood trauma and lifetime AVH, but not when other variables were included within analyses (Shah et al., 2014; Sommer et al., 2010) or when sensitivity analyses were conducted with a subgroup of participants in which symptoms were validated by interview (Van Nierop et al., 2014).

Combined or cumulative effects

Evidence of a cumulative or combined effect of childhood trauma on AVH was reported in five studies. A significant dose-response effect was found, with the probability of experiencing lifetime AVH increasing significantly in those who reported multiple types of childhood trauma (Shevlin et al., 2011). Abajobir et al (2017) found that childhood emotional abuse and childhood neglect combined with other types of childhood trauma were associated with auditory hallucinations. In support of this, significant associations were found between lifetime and severity of auditory hallucinations in those who had experienced more than three (Prokopez et al., 2018) or four (Prokopez et al., 2020) adverse childhood experiences compared to those who had experienced a lower amount. A cluster analysis also showed that the "multi-trauma" cluster consisting of mostly clinical participants with higher levels of most trauma subtypes experienced AVH as having a greater amount of negative content, rated voices as more omnipotent and reported less control over their voices compared to clusters who had experienced lower levels of trauma/less trauma subtypes (Begemann et al., 2021). However, Hardy et al (2016) did not find evidence of combined or cumulative effects of childhood physical, sexual and emotional abuse in any combination on current auditory hallucinations.

Are any subtypes of childhood trauma more strongly associated with AVH?

Childhood Physical Abuse

Of eighteen studies reporting findings about the relationship between childhood physical abuse and AVH, six found support for this relationship, nine did not and three found mixed results. Most were assessed as being Fair or Good in quality, whilst two that found no association were rated as Poor.

Significant correlations and associations were found between physical abuse and lifetime auditory hallucinations (Berg et al., 2015) lifetime AVH (Freeman & Fowler, 2009; Shevlin et al., 2011) and physical abuse was found to significantly increase the risk of lifetime AVH (Shevlin et al., 2011). In another study (Sommer et al., 2010) participants experiencing AVH reported significantly more physical abuse in childhood. However, although significant associations were found between physical abuse and lifetime AVH in two further studies (Sheffield et al., 2013; Van Nierop et al., 2014), these results were no longer significant when controlling for depression or in sensitivity analyses respectively. Where it was possible to extract effect sizes, small effects were found across all studies finding evidence for a relationship between physical abuse and AVH. Most of the studies that found a significant association recruited non-clinical samples (n = 4) whilst one recruited a mixed sample (So et al., 2016) and another recruited a clinical sample (Berg et al., 2015). Another study recruiting a mixed sample found a significant correlation between physical abuse and auditory hallucination proneness in the non-clinical sample, but not in the clinical sample within this study (Goldstone et al., 2012).

In contrast, nine studies found no significant correlations or associations between physical abuse and auditory hallucination severity (Akbey et al., 2019; Hardy et al., 2016; Kim et al.,

2018) or lifetime AVH types (Misiak et al., 2016) and some studies found that physical abuse did not predict the presence of current auditory hallucinations (Mason et al., 2009) or AVH (Daalman et al., 2012). One study (Rajkumar, 2015) found no difference in physical abuse scores between those who experienced auditory hallucinations and those who did not, and another (Üçok & Bikmaz, 2007) found no difference in auditory hallucination severity between those who reported physical abuse compared to those who had not. However, these two studies had relatively small sample sizes and one received a quality rating of "Poor". Similarly, physical abuse was not associated with an increased risk of auditory hallucinations in the longitudinal study (Abajobir et al., 2017). Most studies that did not find an association recruited a clinical sample (n = 7), whilst one recruited from the general population (Abajobir et al., 2017) and another recruited a mixed sample (Daalman et al., 2012).

Childhood Sexual Abuse

Of twenty-four studies reporting findings for the relationship between childhood sexual abuse and AVH, ten found evidence for a relationship, six did not and eight found mixed results. Six of the studies finding a significant relationship between sexual abuse and AVH were rated as Fair and four were rated Good in quality. Of the studies finding mixed results, six were rated as Fair and two as Poor in quality. Of the studies that did not find an association, three were rated as Poor in quality, two were rated as fair but had smaller sample sizes and one was rated Good.

Significant correlations and associations between sexual abuse and current auditory hallucination severity (Akbey et al., 2019), lifetime AVH (Berg et al., 2015; Misiak et al., 2016) and the presence of auditory hallucinations (Hardy et al., 2016) were reported with small effect sizes, ranging from 0.13-0.24. However, in one higher quality study (Misiak et

al., 2016) when analysing genders separately, this relationship was only found in females, with a medium effect size. In another study, sexual abuse was only correlated with auditory hallucination proneness in the clinical, but not the non-clinical sample (Goldstone et al., 2012). Sexual abuse was found to be significantly associated with lifetime AVH (Van Nierop et al., 2014) and this was the only subtype of childhood trauma in which this association was confirmed in a sensitivity analysis in a subgroup of participants in which symptoms were validated by interview (Van Nierop et al., 2014).

Significantly higher rates of childhood trauma were found between participants who reported experiencing AVH, compared to those who did not (Begemann et al., 2021; So et al., 2016; Sommer et al., 2010). Similar results were found for lifetime auditory hallucinations when controlling for depression (Sheffield et al., 2013). Sheffield et al (2013) also found that abuse subtypes together predicted lifetime auditory hallucinations, but this was not found in a subgroup of people who experienced physical and emotional abuse without sexual abuse. This led the authors to conclude that sexual abuse was a specific risk for auditory hallucinations. However, when conducting a MANOVA including other childhood trauma subtypes, the same study found that lifetime auditory hallucinations did not predict the reporting of childhood sexual abuse.

Childhood rape was also found to be associated with lifetime AVH in two studies (Freeman & Fowler, 2009; Shevlin et al., 2011). The latter study found that experiencing childhood rape, but not other forms of sexual abuse, increased the probability of experiencing AVH in adulthood. One study using the BBTS found that medium not high betrayal sexual abuse predicted lifetime auditory hallucinations (Gómez et al., 2014).

Most studies did not find evidence that sexual abuse is associated with cognitive, behavioural and affective responses to voices assessed using the PSYRATS and the BAVQ (Daalman et al., 2012; Offen et al., 2003; So et al., 2016). One poorer quality study (Andrew et al., 2008) did find that sexual abuse together with other variables (current PTSD symptoms and number of lifetime traumatic events) predicted beliefs about the malevolence, benevolence and omnipotence of voices, but sexual abuse was not a significant predictor alone. Another poorer quality study found a negative correlation between the age at onset of sexual abuse and malevolence of voices with a large effect size (Offen et al., 2003).

Six studies found no evidence for a relationship between sexual abuse and auditory hallucinations. In clinical samples, no correlation between sexual abuse and auditory hallucination severity was found (Kim et al., 2018) and sexual abuse was found not to predict the presence of current auditory hallucinations (Mason et al., 2009). No significant differences were found in sexual abuse scores between those who did and did not experience auditory hallucinations (Rajkumar, 2015) and no significant differences were found in the severity of auditory hallucinations (Sporle et al., 2011; Üçok & Bikmaz, 2007) in participants who did and did not report sexual abuse. Also, in a non-clinical sample sexual abuse was not found to be significantly associated with increased risk of auditory hallucinations at 21 years of age (Abajobir et al., 2017).

Childhood Emotional Abuse

Of nineteen studies that investigated the relationship between childhood emotional abuse and AVH, eight found evidence for this relationship, six did not and five found mixed results. Seventeen studies were assessed as Fair or Good in quality with the exception of two studies

that did not find a significant association, which received a rating of Poor (Mason et al., 2009; Rajkumar, 2015).

Emotional abuse was found to increase the risk of auditory hallucinations at 21 years of age in a longitudinal study (Abajobir et al., 2017). Significantly higher rates of emotional abuse were found in clinical and non-clinical participants experiencing AVH and auditory hallucinations compared to those who did not (Begemann et al., 2021; Daalman et al., 2012; Sheffield et al., 2013; So et al., 2016; Sommer et al., 2010) and significantly more auditory hallucinations and voices commenting were found in those who reported emotional abuse (Üçok & Bikmaz, 2007). However, this result was not found for auditory hallucinations when controlling for depression in one study (Sheffield et al., 2013). Also, lifetime AVH were found to be significantly associated with emotional abuse, but not in a sensitivity analysis (Van Nierop et al., 2014). Significant positive correlations were reported between emotional abuse and auditory hallucination proneness in a non-clinical but not clinical sample (Goldstone et al., 2012) and another study with a clinical sample (Berg et al., 2015) found that hearing voices conversing was positively correlated with emotional abuse, but not lifetime AVH or hearing one voice. Additionally, significant correlations were found between perceived voice power and criticism (Connor & Birchwood, 2012) but these results were not replicated in another study (Daalman et al., 2012). It was not possible to calculate effect sizes in the majority of these studies, but small to medium effect sizes were found in studies in which effect sizes could be computed.

Six studies found no evidence of a relationship between emotional abuse and auditory hallucinations. These studies reported no significant correlations between sexual abuse and auditory hallucination severity (Akbey et al., 2019; Kim et al., 2018) and lifetime AVH types

(Misiak et al., 2016) and no significant associations between emotional abuse and auditory hallucination (Hardy et al., 2016). Also, in two studies assessed as poor in quality, no differences in emotional abuse levels were found between participants who experienced AH and those who did not (Rajkumar, 2015) and emotional abuse was found not to predict the presence of auditory hallucinations (Mason et al., 2009).

Neglect

Fifteen studies reported results relating to the relationship between neglect and auditory hallucinations of which three found an association, nine did not, and three found mixed results. Most studies received a rating of Fair, whereas two received a rating of Good (Abajobir et al., 2017; Sommer et al., 2010) and one study that did not find an association was assessed as Poor in quality (Rajkumar, 2015).

Neglect was found to be significantly associated with increased risk of auditory hallucinations at 21 years of age (Abajobir et al., 2017) in a higher quality study. In one study, a significant positive correlation between physical, but not emotional neglect was found (Berg et al., 2015) whereas in another, emotional neglect was significantly associated with lifetime AVH (Van Nierop et al., 2014), but this association was not significant in sensitivity analyses. However, significant positive correlations were found between hearing voices conversing and both physical and emotional neglect (Berg et al., 2015). In addition, Sommer et al (2010) found significantly higher rates of emotional neglect, but not physical neglect in participants reporting AVH in a non-clinical sample. Where calculations were possible, all effect sizes were small.

Nine studies did not find evidence of an association. For example, neglect was found not to be significantly correlated with current auditory hallucination severity (Akbey et al., 2019; Galletti et al., 2017; Kim et al., 2018), or associated with AVH severity (Rosen et al., 2020) and no differences were found in auditory hallucination severity in those who reported neglect compared to those who did not (Üçok & Bikmaz, 2007). No differences were found in neglect scores between those who did and did not experience auditory hallucinations in a clinical sample (Rajkumar, 2015) and between AVH in clinical and non-clinical groups and healthy controls (Begemann et al., 2021). Additionally, the presence of lifetime AVH did not predict whether a participant had experienced neglect in one study (Sheffield et al., 2013), whilst neglect did not predict the presence of AVH in another (Daalman et al., 2012).

Interpersonal trauma

Significant positive correlations were found between childhood interpersonal trauma and frequency (Pearce et al., 2017) and severity (Galletti et al., 2017) of AVH. Similarly, a significant positive correlation was found between AVH severity and exposure to environmental violence in childhood (Galletti et al., 2017) with small effect sizes.

Non-victimisation

In one study (Misiak et al., 2016) "general trauma" (which included non-victimisation events such as natural disasters, illness and bereavement) significantly positively correlated with lifetime AVH. However, this was not significant when genders were analysed separately and other studies found no significant association between lifetime AVH and bereavement or growing up in foster care (Van Nierop et al., 2014) or between the presence of auditory hallucinations and childhood non-victimisation events (Hardy et al., 2016).

Does the relationship exist in both clinical and non-clinical samples?

All studies that investigated the relationship between childhood trauma and AVH in non-clinical (n = 8) and mixed samples (n = 5) found an association in total childhood trauma scores and/or at least one type of childhood trauma. Similarly, most studies that recruited a clinical sample found a significant association (n = 18) with the exception of five studies recruiting clinical samples finding no association. As previously mentioned, four of these studies were of poorer quality and all had lower sample sizes, questioning the validity and generalisability of these findings. With regard to childhood physical abuse, differential results were found for studies recruiting clinical and non-clinical samples, with studies recruiting clinical samples generally finding no association and those with non-clinical samples generally finding a significant association, but not exclusively. Within all other subtypes of childhood trauma, studies recruiting both clinical and non-clinical populations appeared to show similar patterns of results.

Do any other variables mediate the relationship?

Eight studies found evidence of other variables mediating the relationship between total childhood trauma and AVH, with most investigating the mediating effects of post-traumatic processes. Dissociation was the most studied mediating variable and dissociation was found to mediate the relationship between childhood trauma and AVH proneness (Bortolon & Raffard, 2018) and with current auditory hallucinations in simple mediation analyses, with specifically depersonalisation mediating this relationship in multiple mediation analyses (Perona-Garcelán et al., 2012). Childhood physical abuse was found to have an indirect impact on auditory hallucination proneness through dissociation, with dissociation and maladaptive schemas (such as subjugation and vulnerability) being found to mediate the relationship between auditory hallucination proneness and childhood emotional and sexual

abuse (Bortolon et al., 2017). Also, Pearce et al (2017) found that dissociation, but not fearful attachment mediated the relationship between childhood interpersonal trauma and AVH frequency. Additionally, Hardy et al (2016) found that post-traumatic avoiding and numbing and hyperarousal, but not intrusive trauma memory or negative other beliefs mediated the relationship between childhood sexual abuse and auditory hallucinations.

Three studies investigated mediating processes that were not related to post-traumatic processes. For example, Pilton et al (2016) found that anxious attachment mediated relationship between childhood sexual abuse, emotional abuse and physical neglect with auditory hallucination severity. Rosen et al (2020) found that dialogic inner speech mediated the relationship between childhood trauma, household dysfunction (including parental violence, abandonment and substance abuse) and childhood abuse and AVH severity. Also, Goldstone (2012) found that the relationship between predisposition to auditory hallucinations and sexual abuse and emotional abuse (combined with life hassles) was mediated by cognitive confidence and experiential avoidance.

Discussion

The current systematic review aimed to summarise and synthesise research investigating the relationship between childhood trauma and AVH in clinical and non-clinical populations. After a systematic review of the literature, thirty-six studies were included in the review. The main findings in relation to the research questions are summarised and implications of these findings for theory and practice are discussed including the identification of future areas of research. Finally, strengths and limitations of both the identified studies and the current review are considered.

Summary of findings

Is childhood trauma associated with AVH in adulthood?

The current review found evidence of a clear significant and positive association between childhood trauma and AVH in adulthood, with small to medium effect sizes, with the most robust evidence existing when total childhood trauma was assessed. Thirty-one of the included studies found evidence of a relationship between AVH and either total childhood trauma scores and/or at least one subtype of childhood trauma, although it is important to consider that possible publication bias could have influenced findings. Some studies found evidence of a significant relationship between childhood trauma and AVH when controlling for confounders, lending support for the specificity of this relationship. More tentatively, there is an indication that there may be a dose-response relationship, with a cumulative/combined effect of trauma types being found in some studies suggesting that experiencing multiple types of childhood trauma may have a stronger relationship with AVH. Generally, higher quality studies found a significant association between childhood trauma and AVH, whilst studies finding no association and tended to be poorer in quality and had smaller sample sizes, which questions the validity and generalisability of their findings and suggests stronger evidence for the existence of this relationship. These findings are similar to previous meta-analyses, which have demonstrated that experiences of childhood trauma are associated with positive symptoms of psychosis in clinical samples (Alameda et al., 2021; Bailey et al., 2018). Therefore, the current review extends these findings to suggest that AVH specifically are also associated with childhood trauma across the continuum.

Are any subtypes of childhood trauma more strongly associated with AVH?

Mixed results were found when investigating the effects of specific subtypes of childhood trauma, with stronger evidence being found for the association between AVH and childhood

abuse subtypes and childhood interpersonal trauma and, more tentatively, neglect with mainly small effect sizes being found across subtypes. However, very little evidence was found for the association between non-victimisation events and AVH. When exploring subtypes of childhood trauma, sexual abuse was the most studied subtype and the most consistent evidence was found for this relationship, supporting previous literature suggesting that sexual abuse may be particularly linked to AVH (McCarthy-Jones, 2011). However, effect sizes were small and thus not larger than effect sizes found in other childhood trauma subtypes, suggesting that childhood sexual abuse is not more strongly associated with AVH than other childhood trauma subtypes. Small to medium effect sizes were found for the relationship between childhood emotional abuse, suggesting a stronger relationship. However, evidence was less consistent for this subtype, as well as physical abuse with some studies of higher quality finding no association, which limits the extent to which conclusions can be drawn about this relationship. Most studies investigating the associations between childhood neglect and AVH found no association, suggesting the evidence for this relationship is somewhat weak. These findings are broadly in line with previous meta-analyses, which found that childhood trauma abuse subtypes are associated with the positive symptoms of psychosis, but found that neglect is more associated with the negative symptoms of psychosis (Alameda et al., 2021; Bailey et al., 2018). However, Bailey et al (2018) did report a significant association between neglect and hallucinations (including non-auditory hallucinations). Therefore, the current findings in the context of previous research suggests that childhood abuse subtypes are associated with positive symptoms of psychosis including AVH and, more tentatively, that childhood neglect may be associated with hallucinations including AVH specifically, but perhaps not with other positive symptoms of psychosis.

Does the relationship exist in both clinical and non-clinical samples?

The current review found extensive support for the relationship between childhood trauma and AVH in both clinical and non-clinical samples. This suggests that this relationship exists and is broadly similar across the continuum of AVH supporting theories of the continuum models of psychosis (Johns & Van Os, 2001; Larøi, 2012; Strauss, 1969). This highlights the value of recruiting non-clinical samples as an important avenue of research into possible etiological mechanisms of AVH. When examining subtypes of childhood trauma, similar associations with AVH were found for most subtypes in clinical and non-clinical samples, suggesting that the relationship between individual subtypes of childhood trauma and AVH also exist across the continuum. However, disparities were found for physical abuse, with significant associations being found with AVH in predominantly non-clinical samples, rather than clinical samples, bringing into question whether physical abuse is specifically associated with AVH in adulthood within healthy voice hearers rather than in clinical populations. However, studies finding no association within this subtype tended to have smaller sample sizes than studies finding an association, increasing the risk of a Type II error within these studies, which could have impacted findings. Thus, further research is required to explain and clarify these findings.

Do any other variables mediate the relationship?

Most studies did not explore the effect of mediating variables in the relationship between childhood trauma and AVH, with only eight studies exploring mediating factors. The most studied mediating variables were related to post-traumatic processes, most commonly dissociation. Other variables such as anxious attachment, maladaptive schemas, dialogic inner speech and cognitive confidence and experiential avoidance were found the mediate

this relationship but only in individual studies. This has implications regarding potential mechanisms involved in the development of AVH following childhood trauma, but suggests that further research is required to identify mediating variables in the relationship between childhood trauma and AVH.

Theoretical implications and future research

This review found evidence of a relationship between childhood trauma and AVH. However, the dominant use of cross-sectional designs employed within most included studies within the review mean that causal conclusions cannot be made, as cross-sectional designs rely on retrospective self-report. Indeed, although the time between childhood trauma exposure and AVH symptoms in adulthood is sufficient to see an effect, it cannot be assumed that childhood trauma exposure preceded AVH, therefore conclusions regarding temporal relationships can only tentatively be made. One longitudinal study was included in the current review, however, baseline measurements of AVH were not collected. Thus, further longitudinal research is required in this area with AVH being measured at multiple time points from childhood to adulthood to examine the extent to which AVH may develop following childhood traumatic experiences. Research of this nature would be more able to identify whether this relationship is causal.

Mixed results were found for the relationship between subtypes of childhood trauma, particularly neglect, prompting the need for future research to clarify this relationship. However, there has been a suggestion within the literature that rather than investigating the individual relationships between specific childhood trauma subtypes and their associations with AVH it could be more beneficial to investigate the combined effects of childhood trauma types in relation to AVH (Trauelsen et al., 2015). This is due to childhood trauma

subtypes often being highly correlated as specific subtypes of childhood trauma rarely occur in isolation, with individuals likely having experienced different combinations of traumas (Jacobs et al., 2012). Thus, analyses investigating individual subtypes in opposition to others, rather than exploring their shared effect could be problematic. This is because it could be concluded that specific types of childhood trauma are not associated with AVH within individual studies, whilst perhaps neglecting the combined effects of these trauma types (Trauelsen et al., 2015). This could perhaps explain the mixed results found for all subtypes of childhood trauma within this review and provides an argument that the shared effect of adversities could be an important focus for future research, which could extend findings from this review which was suggestive of a combined/cumulative effect of childhood trauma on AVH. Conversely, if looking at the individual effect of specific subtypes of trauma, different statistical methods have been suggested, such as hierarchical regression to partial out other subtypes (Bailey et al., 2018) and mixed effects models when including multiple outcomes (Van Nierop et al., 2014), which could provide more robust evidence for specific effects.

The current review provides provisional support for theories that post-traumatic processes are involved in the relationship between childhood trauma and AVH (Bentall et al., 2014; Steel, 2015; Steel et al., 2005), with post-traumatic symptoms such as dissociation being found to mediate the relationship between childhood trauma and AVH. Other variables were found to mediate this relationship, however, so there are likely other mechanisms involved. Therefore, there is a clear need for further research to identify the mechanisms involved in this relationship as this could lead to the development of more specific interventions. Indeed, not all who develop AVH have experienced childhood trauma and given that even the largest effect sizes found in included studies within the current review were still modest, multiple mechanisms are likely to be involved in the development of AVH. Other factors such as

genetics and drug use may also increase vulnerability to developing AVH in adulthood (Wainberg et al., 2021).

Finally, there were limited studies researching the association between non-victimisation events in childhood and AVH, mostly suggestive of a lack of an association, but this should be addressed more widely in future research, with the inclusion of other types of childhood trauma which were not explored within included studies in this review such as bullying. This could lead to a more extensive understanding of a broad range of childhood traumatic events and their relationship with AVH.

Clinical implications

The findings from this review support the current plan within the National Health Service (NHS) to provide a trauma-informed approach within services for people with severe mental health problems (NHS, 2019) which would involve widespread changes at the service level (Sweeney et al., 2018). This could include the careful assessment of trauma in those presenting with symptoms of psychosis, which is recommended by National Institute for Health and Care Excellence (NICE) guidelines (NICE, 2014). However, a recent systematic review concluded that the majority of people who use mental health services are never asked about childhood traumatic experiences, leading to an under identification of childhood trauma in clinical settings (Read et al., 2017). Therefore, it is important for services that provide care to those with symptoms of psychosis to screen for childhood trauma and possible associated PTSD symptoms at assessment. This is especially important as childhood trauma has been found to be associated with increased risk of developing more severe symptoms of psychosis with poorer outcomes (Aas et al., 2016; Bailey et al., 2018;

Mohammadzadeh et al., 2019). Thus, identification of such experiences could be integrated into psychological formulations and targeted in treatment where appropriate.

Current NICE-recommended (NICE, 2014) interventions for AVH include Cognitive Behavioural Therapy for psychosis (CBTp) which focuses on reducing the distress associated with AVH through challenging appraisals of AVH (Morrison et al., 2004). However, if some AVH are linked to trauma-related intrusions it could be valuable to target post-traumatic processes within tailored interventions. For example, it could be beneficial to implement trauma-focused interventions in those whose AVH could be conceptualised as post-traumatic intrusions (Brand et al., 2021), or to tailor CBTp interventions to include psychoeducation about post-traumatic reactions and to challenge any negative appraisals of the trauma experienced (Smailes et al., 2015). It would be valuable for future research to further investigate the extent to which the content of AVH are directly linked to childhood traumatic experiences and to develop and trial tailored interventions targeting the possible trauma-related aspects of AVH.

Strengths and limitations of included studies

The majority of included studies were assessed as Fair in quality. A strength of most studies was the use of valid and reliable measures of AVH and childhood trauma, with the exception of three studies using novel questions to assess for childhood trauma and AVH, which was reflected in the quality assessment of these studies. Most studies used retrospective self-report measures to assess for childhood trauma, for which issues of recall bias, such as the participant's affective state (Colman et al., 2016) or underreporting (Widom & Morris, 1997), could affect accuracy and consistency of reporting. Conversely, a prospective substantiated measure of childhood trauma was used in the longitudinal study. Although this limits recall

bias, it is likely to result in the under identification of participants who may have experienced childhood trauma, which was not disclosed at the time of the trauma, and only identify the more severe experiences (Baldwin et al., 2019). Thus, a combination of both prospective and retrospective measures of childhood trauma would be optimum in future research, although this is often not logistically possible, especially when cross-sectional designs are employed. Also, measures of childhood trauma varied in the reporting period from below 13 to below 18 years of age, which reduces comparability of studies and may limit identification of trauma in those who only measured early childhood trauma. Therefore, it would be beneficial for future research to measure a more consistent reporting period. Also, there were a lack of studies investigating certain types of childhood trauma such as bullying and non-victimisation events, which could be an area of investigation for future research.

The range of measures employed by studies allowed for a broad range of AVH severity and frequency to be assessed, as well as phenomenological characteristics of voices. Interviewer-rated measures were used predominantly which are thought to be more reliable than self-report questionnaires in clinical samples due to cognitive deficits associated with psychotic disorders having the potential to influence responses (Ratcliff et al., 2011). However, the use of varied measures, assessing different elements of AVH, ranging from lifetime presence to current severity could have led to mixed results found and made studies less comparable. Also, assessing AVH at one time point limits the reliability of such assessments as AVH severity and frequency can vary over time.

Cross-sectional designs were used within most of the included studies, limiting the ability to make causal inferences as these designs rely on retrospective self-report. Sample size justifications and power calculations were not reported in most studies with some studies

having low sample sizes. This could explain why some studies found no association between childhood trauma and AVH as this could increase the risk of a Type II error. Future studies should ensure that any analyses used are sufficiently powered and should employ more longitudinal designs to address these methodological concerns. Also, half of the included studies did not control for potential confounds, which beings into question the specificity of the relationship between childhood trauma and AVH. Gender differences in the relationship between childhood trauma and AVH were found in some studies, suggesting that gender may be a confound in this relationship. Also, due to differing time between exposure and outcome, the age at which AVH are measured may also confound this relationship. Therefore, variables such as age and gender should be controlled for in future studies.

Finally, most studies were conducted in Western countries which limits the generalisability of findings to non-western populations. Future research should seek to recruit more culturally diverse samples, which is especially important as prevalence rates for hallucinations are reported to be higher in certain ethnic groups, with Hispanic and Black groups reporting the highest rates of auditory hallucinations (Beavan et al., 2011).

Strengths and limitations of the current review

The current review has several strengths. It is the first review to explore the relationship between AVH and childhood trauma in clinical and non-clinical samples, leading to a comprehensive review of this area of research. Also, the inclusion of a second reviewer on a proportion of the studies in both stages of the screening, and the detailed quality assessment, reduced methodological errors and assessor bias.

There are, however, limitations to the current review. The review included studies measuring auditory hallucinations, which could include non-verbal auditory hallucinations and thus findings should be viewed with some caution. However, as AVH are the most common type of auditory hallucination (American Psychiatric Association, 2013; Nayani & David, 1996), and these terms are often used interchangeably, these studies are likely to have yielded findings predominantly related to AVH. Also, clinical samples consisted of those with diagnoses of a psychotic disorder and excluded studies recruiting other clinical samples such as personality disorder and bipolar in which AVH can occur, therefore, it did not assess whether the relationship between childhood trauma and AVH exists in populations with other diagnoses. However, including studies with other clinical diagnoses was likely to have confounded the results of the review due to different clinical profiles present within these mental health problems, thus excluding studies recruiting participants with non-psychosis diagnoses allowed a clearer synthesis of the association between childhood trauma and AVH. However, future research could focus on determining whether findings of the current review are replicated in AVH associated with other diagnoses. Also, information about comorbid diagnoses and medication use was not extracted in the current review from studies in which this information was reported and thus were not taken into consideration during data synthesis. These variables could have presented a confound in included studies which measured current experiences of AVH and so any future systematic reviews in this area should consider the effect of these variables on the relationship between childhood trauma and current AVH. Although effect sizes were calculated where possible, allowing for comparability of effects across some studies this was not possible for all studies, for example where relevant statistics were not reported, thus reported effect estimates in relation to findings should be interpreted with caution. Also, although the quality assessment tool allowed for a thorough assessment of the internal validity of studies, it did not extensively

address some factors that are likely to contribute to methodological quality such as selection bias. The review did not include unpublished or grey literature and reference lists of included studies were not searched, which could have limited the scope of the review, although the systematic nature of this review with the search of four different databases provided a thorough review of the available peer-reviewed literature. Finally, as the review included studies available in the English language, it is possible that relevant research published in other languages was overlooked.

Conclusions

In conclusion, the current review found extensive support for the relationship between childhood trauma and AVH across the continuum of AVH. The most robust evidence exists when total childhood trauma is assessed, with some evidence of a combined or cumulative effect of childhood trauma on AVH. However, there is also substantial evidence for the relationship between AVH and childhood abuse subtypes and interpersonal abuse, although predominantly within non-clinical samples with regard to physical abuse. There is weaker evidence for the relationship between neglect and AVH and little support for the relationship between non-victimisation events with AVH. Further longitudinal research should be conducted to ascertain whether the relationship between childhood trauma and AVH is causal. Findings provisionally support theories that post-traumatic processes may be indicated in the relationship between childhood trauma and AVH and thus the development and trialling of clinical interventions targeting post-traumatic processes could be an important avenue of future research.

Chapter III: Empirical Study: Childhood trauma and language network function in the adult brain; an fMRI analysis

Abstract

Childhood trauma is a risk factor for psychosis and is consistently found to be associated with the experience of auditory verbal hallucinations (AVH) in adulthood. It is possible that childhood trauma may alter brain development trajectories, resulting in brain alterations in adulthood associated with the development of mental health problems including AVH. However, there is little research investigating how childhood trauma affects regions and networks in the brain known to be involved in AVH. Therefore, the current study aimed to explore whether, in high and low childhood trauma groups without psychiatric diagnosis, there were functional differences in brain activation and connectivity during a Semantic Object Retrieval Task – which activates language-related areas of the brain that have previously been associated with AVH. Data from a functional Magnetic Resonance Imaging (fMRI) project was analysed. Fifty-two participants were assigned to High childhood trauma (CT) (n=28) and Low CT (n=24) groups and seven brain regions of interest (ROI) were examined that are associated with the experience of AVH. In the High CT group, higher activation was seen in the right frontal operculum, although in further analyses this group difference was explained by current negative affective states. Participants in the High CT group showed reduced functional connectivity compared to the Low CT group between the right frontal operculum and the left supramarginal gyrus. Also, in the High CT group, some childhood trauma subtypes were associated with altered functional connectivity, but psychosis-like symptoms and psychological resilience were not. Findings could be tentatively suggestive of neural mechanisms associated with the development of AVH following

childhood trauma. This preliminary evidence supports the need for further research in this area, which could advance understanding of how childhood trauma may affect brain development to increase the risk of AVH in adulthood, potentially leading to novel treatments for AVH such as brain stimulation treatments.

Introduction

Childhood trauma is widely experienced, with the World Health Organisation (WHO) estimating nearly 40% of the general population worldwide have experienced a form of childhood trauma (Kessler et al., 2010). Childhood trauma is generally defined in the literature as being exposed to potentially traumatic events before the age of 16 or 18 years (Alameda et al., 2021). These traumatic events include childhood physical, sexual and emotional abuse and physical and emotional neglect, as well as bullying, and non-victimisation events such as illness and natural disasters (Spalletta et al., 2020). Childhood trauma has been the focus of extensive research examining etiological factors for a variety of mental health problems and has been found to be significantly associated with many psychiatric disorders in adulthood, including depression, bipolar disorder and anxiety (McKay et al., 2021). Notably, extensive evidence exists that childhood trauma is associated with the experience of psychosis in adulthood. Meta-analyses have provided evidence to suggest that childhood trauma is a substantial risk factor for the development of psychosis (Matheson et al., 2013; Varese et al., 2012), with an estimated population attributable risk of 33% (Varese et al., 2012) and a 10-fold increased risk of being prescribed antipsychotic medication in adulthood (Anda et al., 2007). Research has found that childhood trauma is not only associated with an increased risk of psychosis, but also with increased severity of symptoms such as hallucinations (Bailey et al., 2018) and poorer outcomes (Aas et al., 2016) within psychosis populations.

More specifically, childhood trauma has consistently been found to be associated with individual symptoms of psychosis, such as auditory verbal hallucinations (AVH) in those with and without an accompanying diagnosis of schizophrenia spectrum disorders. AVH or "hearing voices" are terms used to describe the experience of hearing voices in the absence of corresponding external stimuli, which commonly causes the individual distress and of which the individual feels they have little control over (Larøi et al., 2012). AVH are highly prevalent in those with a psychotic disorder, with an estimated 74% prevalence in those with a diagnosis of schizophrenia (Bauer et al., 2011). Many studies have found a significant relationship between childhood trauma and AVH in adulthood within clinical and non-clinical populations (Begemann et al., 2021; Prokopez et al., 2018; Shevlin et al., 2011; Sommer et al., 2010; Van Nierop et al., 2014), with childhood sexual abuse often reported as being more strongly associated with AVH than other types of trauma (Daalman et al., 2012; McCarthy-Jones, 2011; Sheffield et al., 2013). Although much of this evidence is associative or correlational in design and thus cannot indicate a direct causal relationship (Bentall & Varese, 2012), it does suggest that childhood trauma can contribute to the development of AVH in adulthood.

However, it is unclear exactly how childhood trauma increases the risk of psychosis and, more specifically, AVH. On a neural level, it has been hypothesised that trauma experienced during sensitive periods of brain development such as childhood may alter brain developmental trajectories, resulting in neurobiological brain alterations in adulthood linked to the development of mental health problems (Teicher & Samson, 2016). However, the neural mechanisms through which childhood trauma may affect brain development and increase the risk of developing AVH in adulthood are unclear. Examining these mechanisms

is vital to provide a greater understanding of the mechanisms underlying the development of AVH and potentially identify neural targets for therapeutic intervention. Neuroimaging studies including functional Magnetic Resonance Imaging (fMRI) can provide a way to examine this. fMRI provides an indirect measure of brain activity by detecting local changes in blood flow (the blood-oxygen-level-dependent (BOLD) signal) which are assumed to correlate with the temporal activation of brain regions (Poldrack et al., 2011). fMRI can, therefore, be used to examine potential differences in functional brain activation and connectivity that may be present in populations that have experienced childhood trauma compared to those who have not (Teicher et al., 2016).

Previous neuroimaging studies recruiting various adult psychiatric and healthy samples who have experienced childhood trauma have identified altered structure and function in certain areas of the brain in this population (Paquola et al., 2016; Teicher et al., 2016). A meta-analysis of 38 neuroimaging studies found that structurally, prefrontal-limbic grey matter volumes are altered in psychiatric cohorts with a childhood trauma history compared to psychiatric populations without a childhood trauma history (Paquola et al., 2016). More specifically, those who had experienced childhood trauma exhibited smaller right hippocampus and right dorsolateral prefrontal cortex volumes, compared to those who had not. Functionally, those who have experienced childhood trauma show alterations in activation within regions involved in threat detection and reward anticipation, with increased amygdala response to emotional faces (Dannlowski et al., 2012; van Harmelen et al., 2013) and diminished striatal activation in response to anticipated rewards (Dillon et al., 2009; Hanson et al., 2016) as well as differences in sensory systems and network architecture (Teicher et al., 2016).

Interestingly, a number of studies have found that differences are present in both those who have a psychiatric diagnosis and resilient individuals who experienced childhood trauma but have not gone on to develop a mental health problem in adulthood. For example, reduced hippocampal volume is found within populations with a diagnosis of depression, but is also found within those who have experienced childhood trauma without depression (Dannlowski et al., 2012; Samplin et al., 2013). Also, heightened amygdala response to emotional faces, which is associated with post-traumatic stress disorder and depression has also been found in participants who have experienced childhood trauma without psychiatric diagnosis (Dannlowski et al., 2012). Therefore, it is apparent that some brain changes associated with certain psychiatric disorders are also present in those who have experienced childhood trauma, without psychiatric diagnosis. This has led researchers to hypothesise that there may be adaptive resilience mechanisms present within these individuals that allow them to compensate for the neurobiological consequences of childhood trauma, preventing them for developing mental health problems (Teicher et al., 2016). It also questions whether there are differences within non-clinical populations who have experienced childhood trauma in areas of the brain that are implicated in AVH, which is an area that has not yet been researched.

Neuroimaging research has been conducted to investigate the underlying brain mechanisms of AVH, including structural and functional neuroimaging studies, as well as research into connectivity between brain areas and networks. Two main approaches have been employed within this research, which include “symptom association” (or trait) studies and “symptom capture” (or state) studies (Ćurčić-Blake et al., 2017). Symptom association studies compare brain structure, function and connectivity between participants who experience AVH with those who do not. Symptom capture studies investigate differences in activation within brain regions and networks when participants are experiencing AVH compared to when they are

not, in which participants indicate when they are experiencing AVH whilst undergoing neuroimaging scans.

Within neuroimaging studies, regions and networks associated with language processing have been widely implicated in the experience of AVH, with frontotemporal brain regions generally found to be associated with the experience of AVH. Structurally, areas of the brain associated with language processing networks have been found to be reduced in participants with schizophrenia who experience AVH in symptom association studies. The most consistent evidence includes reduced grey matter volumes in the superior temporal gyrus (STG) and the middle temporal gyrus (MTG) (Allen et al., 2008, 2012; Köse et al., 2018; Modinos et al., 2013). Functionally, a more distributed network of activation including these temporal brain areas as well as frontotemporal language areas have been implicated in the experience of AVH in symptom capture and symptom association studies (Allen et al., 2008, 2012). A meta-analysis conducted on 10 symptom capture studies calculated the activation likelihood to estimate brain areas most consistently associated with AVH (Jardri et al., 2011). This meta-analysis identified multiple brain areas in frontotemporal language areas involved in speech generation and perception, including the Broca's area, anterior insula, precentral gyrus, frontal operculum, STG and MTG and the inferior parietal lobule. These results were largely replicated in a non-clinical sample of participants who experience AVH (Diederen et al., 2012). Also aberrant frontotemporal functional connectivity has been found in a number of studies between frontal, temporal and parietal language-related brain regions (Allen et al., 2012; Ćurčić-Blake et al., 2017). Although there are inconsistencies within this research, with many studies finding reduced functional connectivity and some finding increased connectivity, perhaps due to differing methodologies employed by studies, research tends to suggest that there is aberrant functional connectivity in brain networks associated with AVH.

Intriguingly, structural alterations have also been found in language-related regions of the brain in those who have experienced childhood trauma without psychiatric diagnosis. This includes reduced MTG grey matter volumes in children and adolescents who had experienced childhood trauma compared to those who had not (De Brito et al., 2013) and, in a white matter diffusion tensor imaging (DTI) study, reduced structural connectivity in the STG which connects two language processing areas (Broca's area and Wernicke's area) was found in adults who experienced high levels of parental verbal abuse in childhood (Choi et al., 2009). This suggests it is possible that areas of the language networks implicated in AVH may also be altered in those who have experienced childhood trauma without psychiatric diagnosis. However, functional studies have not yet investigated whether those who have experienced childhood trauma without psychiatric diagnosis also display alterations in activation and connectivity in frontotemporal language areas of the brain.

One way to examine whether there are functional alterations in the language regions and networks of the brain that have been implicated in the experience of AVH, in both clinical (Jardri et al., 2011) and non-clinical populations (Diederen et al., 2012), is to examine whether there are functional differences when completing an experimental task that activates frontotemporal language networks. The Semantic Object Retrieval Task (SORT) is an fMRI experimental task paradigm designed to elicit semantic processing in the form of the recall of an object in semantic memory (Assaf et al., 2006; Kraut et al., 2002). This task has been shown to robustly activate frontotemporal language areas during semantic processing (Assaf et al., 2006), thus, the SORT paradigm provides a robust method to examine this gap in the literature.

The current study

The current study aimed to address knowledge gaps in the neuroimaging research literature by investigating functional changes in language networks associated with childhood trauma. More specifically, it aimed to investigate the possible neural mechanisms through which childhood trauma increases the risk of developing symptoms of psychosis. To do this, it sought to identify whether there are alterations in functional brain activity and connectivity in language regions and networks associated with AVH in a sample without psychiatric illness who have experienced either high or low levels of childhood trauma. The current study is the first to explore this and used the SORT task to activate language areas of the brain known to be associated with AVH. Cognitive measures and a measure of current negative affective state were used to ensure groups were matched on these variables and to allow for analyses to control for these variables if they were not. Any differences found between high and low childhood trauma groups, could increase understanding of the possible brain changes following childhood trauma and provide preliminary evidence of potential neural mechanisms of the development of auditory verbal hallucinations, which could help to identify areas of the brain that could be targeted in treatment.

It was hypothesised that:

1. Relative to a low childhood trauma group, a high childhood trauma group would show altered functional activation in one or more language regions that have been implicated in the experiences of AVH, namely, the Broca's area, anterior insula, precentral gyrus, frontal operculum, STG and MTG and the inferior parietal lobule.
2. Relative to a low childhood trauma group, a high childhood trauma group would show altered functional connectivity in these language regions.

3. In the high childhood trauma groups, measures of childhood trauma, psychological resilience and/or psychosis-like symptoms would be associated with changes in activity and connectivity in language regions.

Methods

The current study analysed data from a wider neuroimaging project investigating brain function and chemistry within a non-clinical sample with high and low levels of childhood trauma as determined by the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003). The recruitment and data collection strategies outlined were carried out by the University of Roehampton. The author was responsible for recruitment and data collection of 43 datasets for this project in a Research Assistant capacity prior to commencing the Doctorate in Clinical Psychology. For the current study, the author developed hypotheses and carried out all data pre-processing and analyses.

Design

A quasi-experimental mixed design, consisting of between-subject variables (IV: high and low childhood trauma (CT) groups) and within-subject variables (IV: SORT task conditions; the identification of Random, Semantic and Null word pairs) was used. Task accuracy scores and reaction times (behavioural measures) and brain activation and connectivity parameters (fMRI measures) were dependent variables. The fMRI element of this project employed an event-related jittered design, where stimuli are presented for short amounts of time with varying interstimulus intervals, allowing for the task to be randomised and minimising potential confounds such as expectation and habituation (Tie et al., 2009).

Participants

Fifty-eight participants were recruited via opportunity sampling from the University of Roehampton and Royal Holloway University of London student Facebook groups. Recruitment for this study comprised two phases. Firstly, an online self-report screening survey including the Childhood Trauma Questionnaire (CTQ) and the Brief Symptom Inventory (BSI) was completed by 230 respondents. Secondly, participants were recruited from the upper and lower quartiles of CTQ score distribution determined by the first 100 respondents of the project to form two distinct groups; a High CT group (CTQ scores >40.5, n = 28) and a Low CT group (CTQ scores <29.5, n = 24). The score range for the CTQ is 25-125. This method has been used in previous studies to create groups based on upper and lower distributions (Morgenroth et al., 2020; Tell et al., 2018) and ensures that groups are distinct in levels of childhood trauma. Previous studies have used similar cut off scores to establish high and low childhood trauma groups (Lee et al., 2017; Kart, & Türkçapar, 2019). Also, all participants within the High CT Group reported levels of childhood trauma above the suggested cut off scores (Bernstein & Fink, 1998) in at least one CTQ subscale, whilst no participants in the Low CT Group reported levels above suggested cut off scores in any CTQ subscale. Inclusion criteria were healthy adults aged 18 years or over with no current or historic diagnosed psychiatric disorder. Exclusion criteria included contraindication for MRI (for example, the presence of metal and pregnancy) and neurological illness. These criteria were assessed via the screening survey. The absence of lifetime psychiatric or neurological conditions was assessed using two questions: “have you ever been diagnosed with a psychiatric condition (e.g., ADHD, depression, anxiety, mood disorders)?” and “Have you ever been diagnosed with a neurological disorder or disease (e.g. epilepsy, stroke, head injury, seizures, brain tumours, brain surgery, Parkinson’s disease)?”. The BSI was conducted at screening so that any potential participants with extreme total scores could be

excluded from taking part in the fMRI element of the project due to this indicating high levels of psychiatric symptoms. However, no screened participants reported extreme BSI scores and thus no participants were excluded on this basis.

Four participants were excluded from the experiment due to problems with running the experimental task during data collection, and a further two participants were excluded due to unusable structural scans which made fMRI data unusable in group analyses. Therefore, the final sample included 52 participants with 28 in the High CT group and 24 in the Low CT group. Participants were 18-26 years of age (M=20.46, SD= 1.77), with 13 participants identifying as male and 39 identifying as female. The sample exceeded suggested group sizes of >20 (Simmons et al., 2011). However, a-priori power analyses were not conducted for the fMRI project, which is a significant limitation to this study. Power analyses are rarely carried out in fMRI studies due to perceived difficulties in carrying out power analyses, such as the lack of robust effect sizes within previous fMRI studies and the cost of conducting an fMRI study with a high sample size (Poldrack et al., 2017). This results in the majority of fMRI studies that are conducted having small sample sizes and thus low power, which questions the validity of results (Szucs & Ioannidis, 2020). In the current study, a post-hoc sensitivity analysis was conducted using GPower software with values of $\alpha = 0.05$ and power = 0.80, which suggested the current study was powered to detect effect sizes of d=0.79 or greater meaning that the current study was unlikely to reliably detect small to medium effects, which increases the risk of a Type II error within this study. The project was granted ethical approval from the University of Roehampton in 2018 (ref: PSYC 18/296) with Professor Paul Allen as the named researcher. Ethical approval for the current project was granted by Royal Holloway University of London Research Ethics Committee on 7th March 2021 (application ID: 2508; see Appendix 2). Informed consent was obtained at all stages and participants were

reimbursed £20 from University of Roehampton for their time in the fMRI element of the project.

Measures

Screening measures

Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003).

The CTQ provides a retrospective measure of childhood abuse and neglect occurring before the age of 18 years. It is a 28-item self-report questionnaire using a 5-point Likert scale (from 1=never true to 5=very often true) with five subscales for different types of maltreatment: physical, emotional and sexual abuse, and emotional and physical neglect. Subscales consist of five questions with scores ranging from 5 to 25. It is a widely used scale and has been found to have good internal consistency reliability coefficients (0.66 to 0.92) and good test-retest reliability coefficients over 4 months (0.79 to 0.86) across a range of samples (Bernstein & Fink, 1998). Factor analyses have confirmed the five subsets in community samples and it has good convergent validity with therapist rating for all subscales, indicating good construct validity (Bernstein et al., 2003; Scher et al., 2001).

Brief Symptom Inventory (BSI) (Derogatis & Melisaratos, 1983).

The BSI was used to measure psychiatric symptoms. The BSI consists of 53 items that are rated on a 5-point Likert scale and encompass nine subsets of psychiatric symptoms: anxiety, depression, psychoticism, paranoid ideation, hostility, phobic anxiety, obsessive-compulsive, somatization and interpersonal sensitivity. In the original administration of the questionnaire, internal consistency coefficients for subsets ranged from 0.71 to 0.85 and test-retest reliability coefficients ranged from 0.68 to 0.91, indicating good reliability. In addition, a factor analysis derived the nine subsets and it displayed high convergent validity with the

Minnesota Multiphase Personality Inventory, indicating good construct validity (Derogatis & Melisaratos, 1983). In the current study, the positive symptom distress subscales (psychoticism and paranoia) were used as correlates of interest to assess whether any functional or connectivity fMRI results were associated with psychosis-like symptoms.

Other measures

Connor-Davidson Resilience Scale (CD-RISC) (Connor & Davidson, 2003).

The CD-RISC was used in the study as a measure of resilience to examine whether resilience was associated with any fMRI effects found. The authors describe resilience as "the personal qualities that enable one to thrive in the face of adversity" and items assess a number of components of resilience including the notion of personal competence, tolerance of negative affect and acceptance of change. It is a self-report questionnaire consisting of 25 items scored on a 5-point scale. The authors reported good internal consistency in the general population (0.89) and good test-retest reliability (0.87). Scores positively correlated with the Kobasa hardiness measure (r=-0.83, p<0.0001) and negatively correlated with the Sheehan Stress Vulnerability Scale (r=-0.32, p<0.0001) indicating good construct validity (Connor & Davidson, 2003).

The Depression Anxiety Stress Scales (DASS) (Lovibond & Lovibond, 1995)

The DASS was used as a measure of current negative affective states of participants. It measures state levels of three "negative" emotional states; depression, anxiety and tension/stress. The DASS is a self-report questionnaire consisting of 42 items, with 14 items in each subscale, scored on a 4-point scale of frequency/severity in which participants are asked to rate to what extent they have experienced symptoms over the past week. Scores range from 0-42 on each subscale, with higher scores indicating higher levels of emotional

states. The DASS demonstrates good internal consistency, with internal consistency coefficients for subscales being reported as 0.91 for Depression, 0.84 for Anxiety and 0.90 for Stress in a student population. Good construct validity was also reported, with the DASS depression subscale positively correlating with the Beck's Depression Inventory (r=0.74) and the DASS anxiety subscale positively correlating with the Beck's anxiety Inventory (r=0.81), (Lovibond & Lovibond, 1995). Total DASS scores (consisting of the sum of all subscales) were used as a covariate of no interest to control for negative affective state in fMRI analyses.

Cognitive Measures

Three cognitive measures were also administered to ensure groups were closely matched for cognitive ability, controlling for potential confounding effects on task-related brain activation. These consisted of the Reading Level 2 from the Wide Range Achievement Test-Revised (WRAT-R; Jastak & Wilkinson, 1984) as a rough IQ estimate, a forward and backward digit span task from the Wechsler Adult Intelligence Scale (WAIS-III; Wechsler, 1997) as a measure of working memory and the F-A-S task as a measure of verbal fluency (Spreen & Benton, 1977).

Demographics

Basic demographics were obtained including gender, age, ethnicity, handedness, current alcohol and tobacco use, current and historic use of cannabis, using an adapted version of the Cannabis Experiences Questionnaire (CEQ; Barkus et al., 2006) and level of education.

Task

Semantic Object Retrieval Task (SORT)

Participants performed a modified version of the SORT whilst undergoing fMRI scans. The SORT taps into a specific form of semantic association by entailing the retrieval of a non-presented specific object from semantic memory storage based on two of its features. Word pairs were presented on the screen, some of which were designed to recall/retrieve a third object (for example "honey-stings" would recall "bee" and "desert-humps" would recall "camel"). Word pair stimuli were obtained by contacting the authors of Assaf et al (2006) and an additional “Null” condition was included as a baseline condition to facilitate fMRI analyses, however, this condition was not of interest in the current study. There were three conditions:

- Semantic: word pairs that are related and recall a third word, such as “honey-stings”
- Random: word pairs that are unrelated, such as “honey-table”
- Null: non-words consisting of asterisks “**** ****”

The conditions were described to participants as “Related”, “Unrelated” and “Non-words” respectively. Word pairs were presented on a screen in the scanner and participants were asked to identify the type of stimulus via button press as fast as possible, with a different button representing each condition. There were 90 trials (30 Semantic, 30 Random and 30 Null) and stimuli were randomised. Words were presented for 3 seconds with a randomised jittered interstimulus interval between trials of 2.5, 4 and 5.5 seconds, where participants were asked to focus on a fixation cross on the screen. Therefore, stimulus onset times varied for each participant, which is likely to reduce habituation effects and increase ecological validity (Harmon-Jones & Beer, 2009). The task lasted 10 minutes and 35 seconds.

fMRI data acquisition

All data were collected by University of Roehampton. Structural and functional MRI images were obtained at the Combined Universities Brain Imaging Centre (CUBIC) at Royal

Holloway University of London using a 3 Tesla Siemens Magnetom TIM Trio MRI Scanner equipped with a Siemens 32-channel head coil. Data were collected between 30th January 2019 to 11th November 2020. Structural images were acquired using a T1-weighted Magnetisation-Prepared Rapid Acquisition Gradient-Echo (MPRAGE) sequence (in-plane resolution= 256 x 256 x 176 slices, voxel size=1mm x 1mm x 1mm, repetition time (TR)=1900ms, TE=3.03, scanning time = approximately 5 minutes) to obtain high resolution anatomical images in order for fMRI data analysis to be carried out. Functional images were acquired using a full-brain, T2*-weighted, gradient echo-planar sequence with 330 volumes (TR =2000ms, In-plane resolution = 2.5 x 2.5, Echo time (TE) =30ms, Field of View (FOV) = 204 x 204 mm, Flip Angle (FA) =78^{o}, Slice thickness: 2.5mm) in order to detect Blood Oxygen Level Dependent (BOLD) signal to measure functional whole brain activation during the task.

Procedure

As stated at the start of this section, the current project involved data analysis only. Thus, the recruitment and data collection strategies outlined were carried out by the University of Roehampton, with the author carrying out all data pre-processing and analyses.

After completing the online screening questionnaires, participants from the lower and upper quartiles of CTQ score distribution were contacted via email to invite them to take part in the fMRI element of the project. Participants were not given details of the selection process or told that the project was investigating childhood trauma prior to participation to avoid influences that this might have had on the results of the study, such as confirmation bias. Ethical considerations of the deception used in the recruitment of participants were addressed in the University of Roehampton ethics application and participants were given a full debrief

following participation and given details of organisations or agencies that they could approach if they required support. Participants attended CUBIC and completed CUBIC screening and consent forms before entering the scanner. They undertook the SORT and another behavioural task as well as undergoing structural and Magnetic Resonance Spectroscopy (MRS) scans. Participants completed an additional behavioural task outside the scanner, as well as self-report questionnaires and cognitive measures. A full debrief was provided after participation.

Data were given to the author and were stored on a password protected external hard drive throughout analysis. Raw fMRI data were kept at CUBIC and fMRI data, behavioural data and demographics were also kept securely in digital format by researchers involved in the project at the University of Roehampton. To protect participant confidentiality, data were anonymised during collection, linked by anonymised ID code.

Statistical analysis

Demographic and behavioural data were analysed using IBM® SPSS Statistics Version 25 for Mac software with a statistical significance threshold of $p<0.05$.

Participant characteristics and demographics

Normality of distribution for continuous data was assessed prior to statistical testing. To compare groups for demographic and study variables, independent t-tests were conducted on continuous variables with normal distribution, Mann-Whitney U tests were employed on variables with non-normal distribution and Chi-square tests were conducted on categorical data.

Behavioural analyses

Reaction time and accuracy data were analysed using 2 (CT Groups: High and Low) x 2 (Task condition: Semantic and Random) mixed two-way analysis of variance (ANOVA) to assess participants' performance in the SORT task and assess for any differences in accuracy and reaction time performance between High and Low CT groups.

fMRI analyses

fMRI data were pre-processed and analysed using the Statistical Parametric Mapping 12 software package. A significance threshold of $p<0.05$ (family wise error (FWE) corrected) was applied in fMRI analyses, which corrects for multiple comparisons and decreases the risk of a Type I error.

Pre-processing

Raw fMRI data were pre-processed for each participant to clean the images for any noise or artefacts that could affect results (such as head motion) and normalise the data to adjust for any intersubject differences in brain size and shape so that group analyses could be performed. Pre-processing involved the following processes. Firstly, manual reorientation of anatomical and functional images was conducted to ensure they roughly matched the template that images would be normalised to. This involved setting the origin of the images as the anatomical landmark of the anterior commissure and reorienting images along the anterior commissure-posterior commissure line. Then, functional images were realigned to correct for any head motion that may have occurred during data collection to reduce motion artefacts. Images were realigned using rigid body transformations that utilise six movement parameters. As functional images have low spatial resolution, they were coregistered to the high-resolution anatomical images to allow for clear visualisation of results. Images were

then normalised to a standardised template of the brain; the Montreal Neurological Institute (MNI) template. This process segments images into tissue classes and warps images so that brain locations between participants correspond to each other, allowing for group comparison. Finally, functional images were spatially smoothed using an 8mm Gaussian kernel to ensure data were more normally distributed and to decrease minor intersubject neuroanatomical differences.

First level analyses

Following pre-processing, first-level analyses were conducted with a general linear model being developed for each participant at each voxel of the brain. Task conditions were modelled using participant-specific stimulus onset times and convolved with the haemodynamic response function to form regressors. To further reduce movement artifacts, six movement parameters were entered into the model as regressors of no interest. Contrasts of parameter estimates of the BOLD signal were then specified for each participant to determine areas of the brain that are more active in certain task conditions.

Second level analyses

To identify regions of specific interest to the hypotheses, all second level analyses were based on the first level contrast of Semantic > Random trials. This was because the results from Assaf et al (2006) showed increased activation in language network when participants were engaged in the Semantic condition relative to the Random condition (Semantic > Random contrast). This contrast was therefore entered into second-level random effects one-sample t-test to examine the main effect of task in the whole sample. To test the first hypothesis, this contrast was also entered into second level random-effects independent sample t-test to

examine any differences in functional brain activation between High and Low CT groups. Analyses were run without covariates initially, then total DASS scores and performance accuracy scores were included in second level analyses separately as covariates of no interest to control for the effects of these variables in the fMRI analyses, due to DASS scores and the accuracy of the task performance significantly differing between groups. Small volume corrections (SVC) were used for seven a-priori regions of interest (ROI), for which an 8mm sphere was specified. These regions of interest were taken from the meta-analysis conducted by Jardri (2011), which identified brain regions most consistently associated with AVH. These consisted largely of language region in left Broca's convolution [–48, 10, 7] the left [–42, 0, 6] and right [44, 6, –4] anterior insula the left precentral gyrus [–54, 0, 14], the frontal operculum [42, 12, –10], the superior and middle temporal gyri [–54, –44, 16] and the left supramarginal gyrus [–52, –20, 15]. GingerAle software was used to convert MNI coordinates from significant peak-level activation to Talairach coordinates, then Talairach Daemon software was used to identify brain regions from these coordinates.

Psychophysiological interaction analyses (functional connectivity analyses)

To test the second hypothesis, Psychophysiological Interaction (PPI) analyses were conducted to establish whether there were any differences in functional connectivity between High and Low CT Groups in the ROIs listed above and the seed region. PPI analyses measure task-specific changes in the relationship between brain activation in the seed region of interest and activation in other areas of the brain (O'Reilly et al., 2012) and thus is a measure of functional connectivity. A common approach to selecting seed regions is to identify the region with the strongest task effect (O'Reilly et al., 2012) and thus, based on the Group

fMRI results (see Results section) the seed region chosen was the right operculum [42, 12, -10] in the Semantic>Random contrast. Only one region was chosen, rather than carrying out PPI analyses for each a-priori ROI found to be associated with AVHs in previous research (Jardi, 2011). This was because using multiple seed regions would result in an increased risk of a Type 1 error. 28 participants were excluded from PPI analyses as they did not show significant activation in the seed region. Therefore, the final groups for the PPI analyses included 24 participants in total, with 11 from the Low CT Group and 13 from the High CT group. Eigenvariate time series of the BOLD signal were extracted from an 8mm sphere around the seed region of interest in each subject. A general linear model was specified for each participant consisting of three regressors: the physiological (the extracted time series), the psychological (Semantic>Random) and the PPI (the interaction of the physiological and psychological) regressor. PPI contrast images were then entered into a second-level random effects independent samples t-test to examine any differences in functional connectivity between the seed region and six other regions of interest. These regions of interest were the same as used in the fMRI group analyses (with the exception of the seed region), from the meta-analysis by Jardri (2011). As in the fMRI Group analyses, analyses were run without covariates initially, then total DASS scores and performance accuracy scores were included into second level analyses separately as covariates of no interest.

Correlation analyses with study variables

To test the third hypothesis, parameter estimates (estimated amplitude of the BOLD response) were extracted for each participant where activation or connectivity in regions of interest was found to be different between groups. Pearson product-moment or Spearman's

rank correlations were then conducted separately for High and Low CT Groups between parameter estimates, CTQ total and subscales, BSI psychoticism and paranoia subscales and the CD-RISC depending on whether variables were normally distributed. Bonferroni corrections were used to correct for multiple testing, meaning the significance threshold was set at <0.006 for correlations.

Results

Sample characteristics

Participant demographics and descriptive statistics for the study's measures separated into High CT and Low CT groups are detailed in Table 1. Most of the 52 participants were female (75%) and from a White ethnic background (79%). Participants had an overall mean age of 20.46 years, all were educated to at least A-level and 88% were right-handed. High CT and Low CT Groups did not significantly differ in age, gender, ethnicity, level of and years in education, cognitive variables, handedness, alcohol, cannabis or tobacco use. By design, the High CT group had significantly higher scores on CTQ total and all subscales. The High CT Group also scored significantly higher on BSI and DASS Total scores and subscales, and significantly lower on the CD-RISC compared to the Low CT Group. DASS total scores were controlled for in analyses, whereas BSI and CD-RISC scores were variables of interest and thus were used in correlational tests to analyse whether they were associated with any fMRI effects found.

Table 3.

Demographic information and study variables for High and Low CT groups (presented as Mean (SD))

	High CT Group (n=28)	**Low CT Group (n=24)**	**Test statistic**	**p-value**
Age	20.79 (1.83)	20.08 (1.64)	t=-1.45	0.155
Gender	M=6, F=22	M=7, F=17	χ^2 =0.41	0.521
Ethnicity	White British=12, White Other=8, Mixed White-Asian=1, Indian=1, Bangladeshi=1, Asian background (other)=2, Chinese=1, Other=2	White British=15, White Other=6, Indian=1, Chinese=1, Other=1	χ^2 = 4.67	0.700
Years in education	15.32 (3.32)	15.08 (3.39)	U=352.00	0.764
Level of education	A-level=12, BSc=15, Msc/MA=1	A-level =12, BSc=11, Msc/MA=1	χ^2 =0.310	0.857
Handedness	R=26, L=2	R=18, L=6	χ^2 =3.17	0.075
Tobacco (cigarettes per day)	0.38 (1.51)	1.55 (3.86)	U=212	0.343
Alcohol (units of alcohol per day)	1.55 (1.95)	1.59 (1.65)	U=312.50	0.658
CEQ	2.04 (3.32)	3.17 (7.21)	U=331	0.921
WRAT-R	75.21 (4.65)	76.58 (5.14)	t=1.01	0.318
Digit Span	17.82 (4.13)	17.58 (5.00)	t=-0.19	0.852
Verbal Fluency	44.07 (10.62)	43.29 (13.00)	t=-0.24	0.813
BSI-Total	64.57 (37.02)	23.75 (16.87)	U=581.50	<0.001***
BSI-Paranoia	1.18 (0.67)	0.68 (0.62)	t=-2.75	0.008**
BSI-Psychoticism	1.32 (0.84)	0.88 (0.75)	U=447.50	0.039*

DASS Total	34.79 (22.09)	14.38 (10.32)	U=546	<0.001***
DASS Depression	8.96 (7.54)	3.33 (3.25)	U=545	<0.001***
DASS-Anxiety	12.04 (9.43)	3.79 (4.06)	U=506.50	0.002**
DASS-Stress	13.79 (7.89)	7.25 (5.43)	t=-3.42	0.001**
CD-RISC	61.75 (18.37)	69.75 (8.87)	t=2.04	0.048*
CTQ-Total	57.18 (12.44)	26.88 (1.45)	t=-12.79	<0.001***
CTQ-Emotional Abuse	14.29 (3.89)	5.71 (0.95)	t=-11.29	<0.001***
CTQ-Physical Abuse	9.71 (4.86)	5.00 (0.00)	U=540	<0.001***
CTQ-Sexual Abuse	7.75 (4.54)	5.00 (0.00)	U=468	0.001**
CTQ-Emotional Neglect	14.75 (3.89)	6.00 (1.41)	t=-11.07	<0.001***
CTQ-Physical Neglect	10.68 (3.61)	5.17 (0.38)	t=-8.03	<0.001***

*= <0.05
** = <0.01
***=<0.001

Behavioural SORT performance

For accuracy, ANOVA results revealed a main effect of CT Group ($F(1, 50) = 4.93$, $p = 0.031$), with the High CT Group (M=82.3% correct, SD=10.5) being less accurate across conditions in their responses than the Low CT Group (M=87.6% correct, SD=11.2). No significant main effects of condition or interactions were found. For reaction times, ANOVA results revealed a main effect of Condition ($F(1, 50) = 100.74$, $p<0.001$), with all participants being quicker to respond in the Semantic condition (M=1.56s, SD=0.24) than in the Random condition (M=1.78s SD=0.25). No significant main effects of CT group or interactions were found for reaction time data. [2]

[2] Additionally, behavioural analyses were run controlling for DASS scores, which did not change the main findings.

fMRI analysis of the SORT: Main Effects

Relative to the Random condition, during the Semantic condition there was significantly greater activation in a number of areas of the brain including the bilateral superior frontal gyri, left middle temporal gyrus, right superior temporal gyrus, bilateral inferior parietal lobule, bilateral caudate, the left hippocampus and right parahippocampal gyrus, left dorsal ACC and posterior cingulate gyrus, right thalamus, left subthalamic nucleus and right precuneus (see Table 4 & Figure 2).

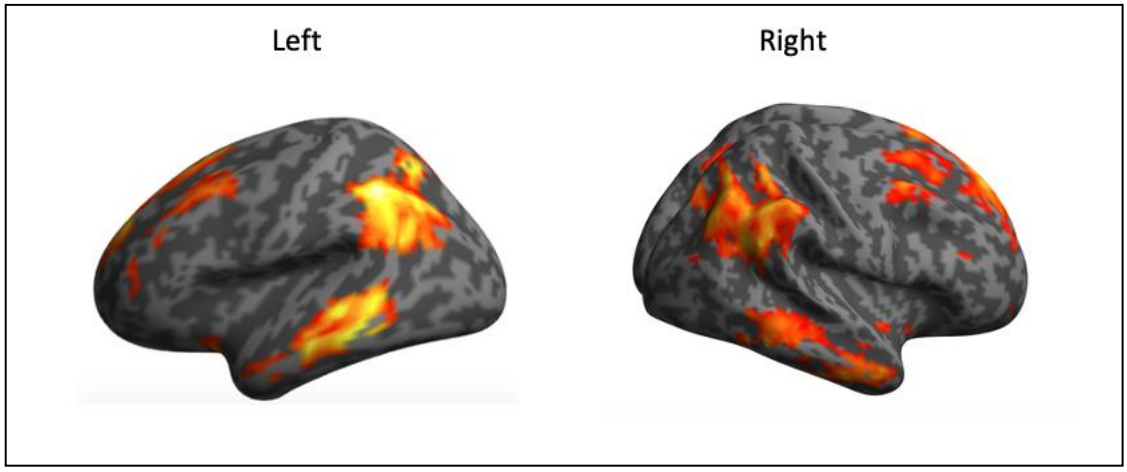

Figure 2.

Statistical parametric maps showing Main Effects of Task in the Semantic < Random contrast. Activation shown at p<0.05 (unc.) for illustrative purposes.

Table 4.

Main effects of task: MNI coordinates and labels of brain areas showing significant increased activation in the Semantic > Random contrast.

MNI Coordinates (mm; x, y, z)			Brain region	Lobe	Brain region (BA)	P (Peak-level FWE-corrected)	Z	k
-6	-46	30	L	Limbic	Posterior Cingulate Gyrus (23)	<0.001	6.71	1719
-46	-50	50	L	Parietal	Inferior Parietal Lobule (40)	<0.001	6.70	1374
-64	-16	-16	L	Temporal	Middle Temporal Gyrus (21)	<0.001	5.94	513
-6	42	4	L	Limbic	Anterior Cingulate (dorsal ACC) (32)	<0.001	5.93	1077
12	-32	4	R	Sub-lobar	Thalamus	0.001	5.54	35
-16	16	64	L	Frontal	Superior Frontal Gyrus (6) (pre-SMA)	0.002	5.46	47
46	-50	30	R	Temporal	Superior Temporal Gyrus (39)	0.002	5.45	106
32	-70	48	R	Parietal	Precuneus (7)	0.005	5.25	188
-12	-10	-14	L	Midbrain	Subthalamic Nucleus	0.005	5.24	15
-26	-28	-10	L	Limbic	Hippocampus	0.006	5.20	11

28	-26	-12	R	Limbic	Parahippocampal Gyrus (28)	0.007	5.26	35
8	14	4	R	Sub-lobar	Caudate Body	0.008	5.13	15
44	-48	52	R	Parietal	Inferior Parietal Lobule (40)	0.008	5.13	124
0	42	54	L	Frontal	Superior Frontal Gyrus (6) (pre-SMA)	0.012	5.05	33
14	46	40	R	Frontal	Superior Frontal Gyrus (8) (pre-SMA)	0.013	5.03	17
-8	10	0	L	Sub-lobar	Caudate Head	0.020	4.93	19

fMRI Analysis of the SORT: Group Effects

Relative to the Low CT Group, during the Semantic > Random contrast, the High CT Group showed increased activation in the right frontal operculum region of interest (x= 42, y=12, z=-10, Z_{peak} = 3.00, pFWE = 0.046; See Figure 3), supporting the first hypothesis. When accuracy scores were included as a covariate of no interest, this difference in activation was still within the significance threshold (pFWE = 0.049). However, when total DASS scores were included as covariates of no interest, this group effect in activation did not meet the significance threshold (pFWE=0.322). There were no significant suprathreshold group effects in any other regions of interest, or in the whole-brain analysis.

Associations between functional activity, childhood trauma and clinical measures

No significant correlations were found between extracted parameter estimates from the right frontal operculum with CTQ total or subscales, BSI psychoticism or paranoia subscales or the CD-RISC in either CT group (See Table 5), meaning the third hypothesis was not supported.

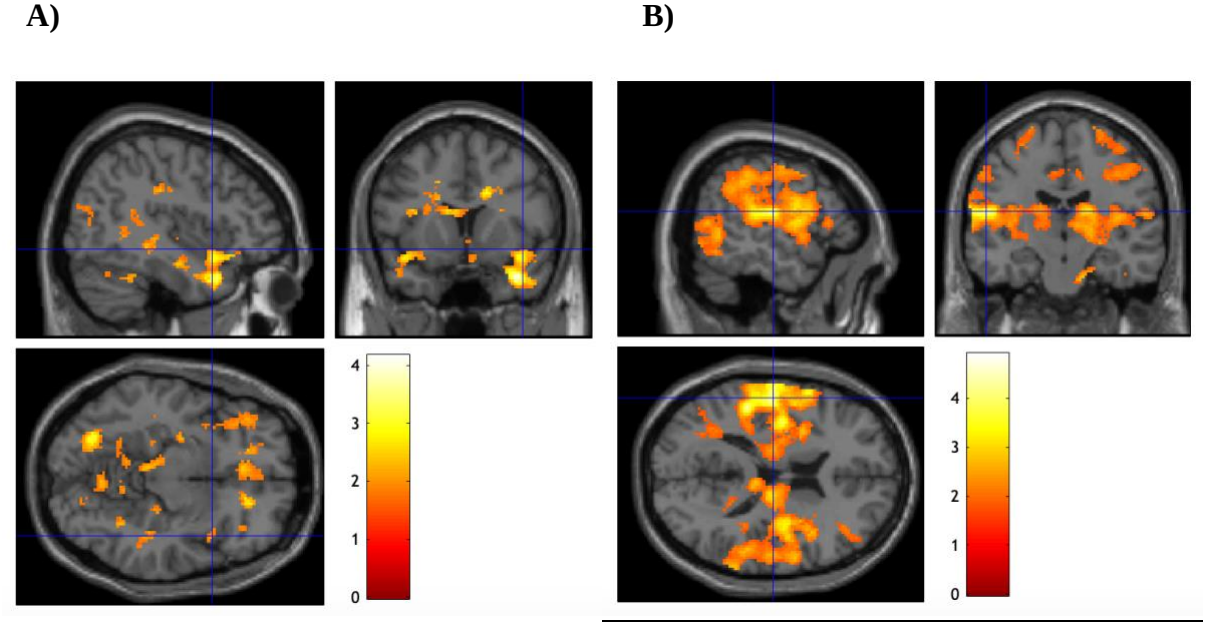

Figure 3.

*Statistical parametric maps showing **A)** increased activation in the right frontal operculum in High CT Group relative to the Low CT Group in the Semantic > Random contrast **B)** reduced functional connectivity between the left supramarginal gyrus and the seed region (right frontal operculum) in High CT Group relative to Low CT Group in the Semantic > Random contrast.*

Functional Connectivity: PPI Effects

The between group comparison of functional connectivity effects (PPI) during the Semantic > Random condition contrast showed that, relative to the Low CT group, the High CT group had reduced functional connectivity between the seed region (the right frontal operculum) and the left supramarginal gyrus (x=–52, y=–20, z=15, Z_{peak}=3.61, pFWE=0.007; See Figure 3). This effect remained significant when accuracy scores were included as a covariate of no interest (pFWE = 0.007) and when total DASS scores were included as a covariate of no interest (pFWE = 0.031), supporting the second hypothesis.

Associations between functional connectivity, childhood trauma and clinical measures

In the high CT group, significant positive correlations were found between PPI parameters in the left supramarginal gyrus and CTQ physical abuse (r=0.80, p=0.001) and emotional neglect (r=0.76, p=0.003) subscale scores. A significant negative correlation was found between PPI parameters in the supramarginal gyrus and childhood sexual abuse subscale (r_s= -0.76, p=0.002). These results support the third hypothesis. No significant correlations were found between PPI parameters in the supramarginal gyrus and CTQ total scores, CTQ physical neglect and emotional abuse subscales, BSI subscales and the CD-RISC within the High CT group. No variables were significantly correlated with PPI parameters within the Low CT group (see Table 5).

Table 5.

Correlations between parameter estimates extracted from Group fMRI analyses and PPI analyses with study variables within High and Low CT groups

Variable	**High CT Group**		**Low CT Group**	
	r	p-value	r	p-value
Group fMRI analysis	*n = 28*		*n= 24*	
Right frontal operculum				
CTQ Total	0.110	0.579	-0.323	0.123
CTQ-Emotional Abuse	-0.112	0.569	-0.124	0.565
CTQ-Physical Abuse	0.242	0.214	^	^
CTQ-Sexual Abuse	r_s = 0.214	0.275	^	^
CTQ-Emotional Neglect	-0.119	0.546	-0.241	0.257
CTQ-Physical Neglect	0.013	0.950	^	^
CD-RISC	-0.129	0.512	-0.074	0.731
BSI-Paranoia	-0.194	0.323	0.172	0.423

BSI-Psychoticism	-0.207	0.290	0.193	0.366
PPI analysis	*n = 13*		*n = 11*	
Left supramarginal gyrus				
CTQ Total	0.650	0.016	-0.165	0.628
CTQ-Emotional Abuse	0.614	0.026	-0.116	0.735
CTQ-Physical Abuse	0.795	0.001*	^	^
CTQ-Sexual Abuse	r_s = -0.764	0.002*	^	^
CTQ-Emotional Neglect	0.756	0.003*	-0.324	0.331
CTQ-Physical Neglect	0.274	0.365	0.391	0.234
CD-RISC	0.049	0.873	-0.088	0.798
BSI-Paranoia	0.007	0.983	0.569	0.068
BSI-Psychoticism	-0.183	0.550	0.523	0.098

^ = correlation could not be conducted due to lack of variability in CTQ subscale scores
*= <0.006

Discussion

The current study aimed to identify whether there were differences in functional brain activity and connectivity in language regions and networks associated with AVH between high and low CT groups in a sample without psychiatric illness. It was hypothesised that there would be differences in functional activation and connectivity in these brain areas between groups and that measures of childhood trauma, psychological resilience and/or psychosis-like symptoms would be associated with any differences in activation and connectivity.

Main findings

The main fMRI effects of the SORT task indicated increased activation in similar language networks as reported in a previous study using this paradigm during the Semantic relative to the Random condition (Assaf et al., 2006). This included the pre-supplementary motor area, which is thought to be involved in the cognitive functions of the semantic object recall process (Assaf et al., 2006; Kraut et al., 2002), the inferior parietal lobule, which is implicated in verbal working memory processes (Jonides et al., 1998), the left middle temporal gyrus, which subserves language and semantic memory processing (Cabeza & Nyberg, 2000) the cingulate gyrus, including the dorsal ACC, which is implicated in detecting errors and conflict when carrying out tasks (Botvinick et al., 2001) and the caudate and thalamus, which are likely to coordinate brain activity in the other identified regions (Assaf et al., 2006; Kraut et al., 2002). In addition, increased activation in other brain regions implicated in language and semantic processing (Binder et al., 2009; Price, 2010) was found in the STG, precuneus, as well as hippocampal and parahippocampal regions. It is possible that these additional areas of increased activation were identified due to more advanced MRI procedures and the current study having a larger sample size than the previous study.

The main behavioural task effects indicated that participants took longer to respond in the Random condition than the Semantic condition overall, which replicates previous research using this task in a non-clinical sample (Assaf et al., 2006). This result was expected as the Random condition asks participants to consider whether two unrelated words are semantically related, which is arguably more challenging and participants may require more time to ensure that the correct response is given than the Semantic condition where participants are presented with two clearly related words. There were no overall differences in accuracy found between the conditions, which is contrary to Assaf et al (2006)'s research

which found reduced accuracy in the Semantic condition. However, as the Random condition is arguably the more challenging condition, it suggests that longer reaction times in the Random condition allowed participants to maintain accuracy in this condition. Therefore, the behavioural and fMRI main effects of the SORT task indicate that participants were fully engaged in the task. It also confirms that language areas of the brain were activated during the task, which allowed for a meaningful group comparison in brain activation and connectivity in these areas of the brain.

Group differences in brain activation in the right frontal operculum were initially found, with increased activation in the right frontal operculum. Although the specific function of the right frontal operculum is unclear, it may be involved in language processing (Grodzinsky & Amunts, 2006) and activation in this region is implicated in the experience of AVH (Diederen et al., 2012; Jardri et al., 2011). However, participants' current affective state, as measured by DASS total scores, appeared to largely explain differences in activation between the High and Low CT Groups in the frontal operculum, leading to no differences being found in activation in this region between High and Low CT groups when DASS scores were controlled for. This suggests that current negative affective states may explain the differences in functional activation found between High and Low CT Groups in this region. Similarly, brain activation in the right frontal operculum did not significantly correlate with CTQ, BSI or CD-RISC scores suggesting that activation in this region is not associated with childhood trauma severity, psychosis-like experiences or with levels of psychological resilience.

However, functional connectivity was found to be reduced between the right frontal operculum and the left supramarginal gyrus in the High CT group, compared to the Low CT group. This result was not explained by participants' negative affective state or accuracy

scores. Although PPI results must be interpreted with caution due to the small sample sizes within these analyses, they tentatively suggest that functional connectivity in areas of the brain associated with AVH is altered in those who have experienced childhood trauma. The supramarginal gyrus is implicated in phonological language processing and verbal working memory (Deschamps et al., 2014) and activation in this region and the right frontal operculum are implicated in the experience of AVH (Diederen et al., 2012; Jardri et al., 2011). In both areas, altered structure has been found in those with schizophrenia spectrum disorders, with reduced grey matter in the right frontal operculum being found in participants with schizophrenia compared to controls (Yüksel et al., 2012) and reduced cortical thickness in the supramarginal gyrus being found to be reduced in a clinical high risk for psychosis sample in those who converted to psychosis, compared to those who did not (Del Re et al., 2021). Previous research has found structural differences in grey matter volume (De Brito et al., 2013) and connectivity (Choi et al., 2009) in language-related areas of the brain in those who have experienced childhood trauma without a psychiatric diagnosis. Therefore, the current study adds to the evidence base, tentatively suggesting that childhood trauma is also associated with differences in functional connectivity within language-related areas of the brain.

Additionally, in the High CT Group, significant associations were found between alterations in functional connectivity (PPI) parameter estimates and the CTQ physical abuse, sexual abuse and emotional neglect subscales, with no significant association being found for CTQ total scores, emotional abuse and physical neglect. These results suggest that reduced functional connectivity between these regions may be associated with specific childhood trauma subtypes. However, contradictory results were found, with sexual abuse being negatively correlated with functional connectivity and physical abuse and emotional neglect

being positively correlated with functional connectivity. Due to the small sample sizes within correlation analyses, these results must be interpreted with caution as outliers can have undue influence on analyses, making results less likely to be replicated (Lemons, 2009). Significant associations were not found between functional connectivity parameter estimates and BSI or CD-RISC scores, suggesting that reduced functional connectivity is not associated with psychosis-like experiences or psychological resilience.

Behavioural results were not of interest in the current study, due to the task being chosen to examine differences in areas of the brain that the SORT paradigm elicits. Rather, behavioural analyses were conducted to explore whether there were differences between groups, so that any differences could be controlled for if they were present. However, it is interesting that group differences were found in task performance, with the High CT group found to be significantly less accurate overall than the Low CT Group. Findings would need to be replicated, but these results could suggest that those with higher levels of childhood trauma may have deficits in semantic object retrieval, although it is unclear why this may be the case, or if the reduced functional connectivity found is related to these behavioural differences in accuracy.

Theoretical and clinical implications and future research

The current study's findings contribute to the neuroimaging research base investigating brain changes associated with childhood trauma. The findings suggest that childhood trauma may be associated with altered activation in frontotemporal language areas of the brain associated with AVH (although current negative affective state could explain these differences) and that childhood trauma is associated with reduced functional connectivity in areas of the brain implicated in AVH. This preliminarily evidence tentatively suggests that there may be neural

mechanisms in language-related areas of the brain associated with AVH that could potentially contribute to increased risk for, or the development of AVH following childhood trauma. This finding provides an argument for further research to be carried out further examining the relationship between childhood trauma and altered function and connectivity in these areas of the brain. The SORT task appeared to robustly activate language-related areas of the brain, suggesting that this task could be used for future research investigating alterations in language related areas of the brain in clinical and non-clinical samples. However, it must be stated that causal claims cannot be made as a result of the findings from the current study and thus it is unclear whether the changes in functional connectivity are a direct result of childhood trauma or whether these changes relate directly to the development of AVH, as a non-clinical sample was used. Therefore, it would be valuable for future research to be conducted in this area and for longitudinal designs to be employed to track brain development in these brain areas in those who have experienced childhood trauma compared to those who do not. Additionally, future research could explore differences in how these brain areas develop in those who go on to develop AVH compared to those who do not. This would allow a greater understanding of the potential neural mechanisms involved.

An interesting result from the current study is that specific childhood trauma subtypes appear to be associated with reduced functional connectivity in AVH-related brain areas, with childhood sexual abuse, physical abuse and emotional neglect found to be associated with reduced functional connectivity with large effect sizes, rather than other childhood trauma subtypes or combined, total childhood trauma. Childhood sexual abuse is often found to be more strongly associated with the experience of AVH in adulthood than other childhood trauma subtypes (Daalman et al., 2012; McCarthy-Jones, 2011; Sheffield et al., 2013). Also, previous neuroimaging research conducted into structural brain differences in those who have

experienced childhood trauma have found the greatest reductions in grey matter in those who have experienced physical or sexual abuse, rather than other childhood trauma subtypes such as neglect or combined childhood trauma (Paquola et al., 2016). It could therefore be valuable for future research to investigate the association between specific subtypes of childhood trauma and brain activation and connectivity in areas of the brain associated with AVH, such as childhood sexual and physical abuse, as different abuse types may be differentially related to neural alterations.

As the current study consisted of a non-clinical sample, any clinical implications must be made tentatively and with caution. However, if the differences in functional connectivity found in the current study are related to the development of AVH, this has implications in possible novel treatments for AVH, such as targeting of these brain regions, perhaps to strengthen connectivity between these two areas of the brain. Brain stimulation treatments such as transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS) could be employed, for which evidence base is growing in the treatment of AVH (Nathou et al., 2019). Interestingly, both the frontal operculum and the supramarginal gyrus have been targeted in a recent TMS study recruiting participants with schizophrenia who experience AVH, in which altered topological patterns in these areas were normalised following TMS, although this was not found to be significantly associated with a reduction in AVH, but rather an improvement in neurocognitive functions (Xie et al., 2022). Also, although no association between psychological resilience and reduced functional connectivity was found, neurobiological resilience mechanisms may still be present in those who experience childhood trauma but do not go on to develop psychiatric symptoms in adulthood (Teicher et al., 2016). Thus, further research in this area is required to distinguish any potential differences in those who have experienced childhood trauma and go on to develop

AVH compared to those who do not as this could have treatment implications, such as strengthening any compensatory brain adaptations that may be present.

Strengths and limitations

A main limitation of the current study relates to the sample size, most importantly within the PPI analyses. Although the sample size for main fMRI group analyses exceeds suggested group sizes of >20 (Simmons et al., 2011), within the PPI analyses, the sample size dropped to n = 11 in one group, which is less than suggested group sizes. This drop in sample size was due to some participants not showing significant activation in the frontal operculum. It is possible therefore that the SORT task does not sufficiently activate this brain area. However, this could also be due to the strict statistical significance threshold employed within analyses, meaning that some subjects may not have met significance threshold for activation in this region. Also, fMRI is associated with considerable intersubject variability, meaning that the same task may not activate the same regions and networks of the brain in all subjects (Mueller et al., 2013; Sugiura et al., 2007).

A common criticism of fMRI research is that studies are largely statistically underpowered due to having small sample sizes (Button et al., 2013; Poldrack et al., 2017; Yarkoni, 2009). Low statistical power reduces the chance of detecting a true fMRI effect, but also decreases the chance of a significant fMRI result reflecting a true effect (Button et al., 2013). In the current study, a-priori power analyses were not conducted, which is a significant limitation. Post-hoc sensitivity analyses indicated that the current study was powered to detect large effects, meaning that the current study was unlikely to reliably detect small to medium effects, increasing the risk of a Type II error. Power analyses in fMRI studies are rarely conducted, with only 3% of studies reporting pre-study power calculations in 2017/8, but it is

advised that fMRI studies should conduct a priori power analyses to ensure that studies are adequately powered and should be a requirement for publication of results (Szucs & Ioannidis, 2020). Therefore, results from the current study should be interpreted with caution and it would be beneficial to replicate the current study with a sample size informed by power analyses to confirm or contradict the results found. Also, multiple ROIs were used, which could increase the risk of a Type I error, due to multiple testing. However, a stringent peak-level FWE-corrected statistical significance threshold was used, which has been found to be very conservative, thus making Type I errors less likely (Eklund et al., 2016).

A strength of the current study is that participants were matched on cognitive profiles and education level. In research recruiting childhood trauma samples there are often differences in childhood trauma populations compared to controls (De Bellis et al., 2002; Teicher et al., 2016), which could confound results. This is also an important problem and confound in studies investigating AVH recruiting psychosis samples (Knight & Silverstein, 2001). Thus, recruiting non-clinical participants from a student sample allowed the study to match CT groups in cognitive ability and education level. However, recruiting a student sample does impact on the generalisability of findings (Henrich et al., 2010). Also, although participants were matched on a lack of psychiatric diagnosis, they did differ on measures of self-reported psychiatric symptomatology and affective state. Current negative affective states in particular were a confound in the group fMRI effects. Thus, it would have been preferable for groups to be matched in psychological profile and future studies could consider carefully matching childhood trauma groups on affective states, although this would be difficult to execute. Also, as childhood trauma is associated with increased psychological symptoms (Van Nierop et al., 2015), matching groups on these variables would make the sample less representative of the population being studied. Also, High and Low CT groups were created using the upper and

lower quartiles of CTQ score distribution in an attempt to ensure that groups were distinct in levels of childhood trauma. However, this extreme groups approach has been criticised as it has been shown to reduce reliability and artificially inflate effect sizes (Preacher, 2015), Therefore, future research could consider using a different method to create groups such as a median split of CTQ scores.

An additional limitation is that the sample consisted of a majority white ethnic female sample, which limits the generalisability of these findings to other ethnic groups, which is particularly relevant to this area of research as other ethnic groups, such as Black and Hispanic groups often report higher rates of auditory hallucinations (Beavan et al., 2011). Therefore, future research should strive to recruit more culturally diverse samples. Also, in the current study, total childhood trauma scores were used to create high and low CT groups and, although the High CT group scored higher than the Low CT group on all childhood trauma subtypes measured, there were lower levels of sexual and physical abuse reported than other trauma types, such as emotional abuse and physical and emotional neglect. Therefore, the sample may not be representative of the types of childhood trauma in which structural brain differences are more commonly found. Future research could focus on the recruitment of samples that have experienced higher levels of these specific childhood trauma types.

Another strength of the current study is the use of valid and reliable measures. However, the current study used a retrospective self-report measure of childhood trauma for which concerns about recall bias such as underreporting of childhood traumatic experiences (Widom & Morris, 1997) or the participant's affective state (Colman et al., 2016) could affect the consistency and accuracy of reporting. Also, BSI subscales were used in the current study

as a measure of psychosis-like symptoms, namely the paranoia and psychoticism scales, which do not have a specific measurement for AVH. This could explain why psychosis-like symptoms were found not to be associated with fMRI effects. Future research in this area would benefit from the inclusion of a more robust measure of subclinical auditory verbal hallucination symptomatology/proneness. For example, the Launay-Slade Hallucination Scale (Launay & Slade, 1981) could be employed, which can be used to measure auditory hallucination proneness in non-clinical samples. This would allow a more robust exploration of whether hallucination-proneness is associated with any fMRI effects.

Conclusions

In conclusion, the current study was the first to explore the possible relationship between childhood trauma and alterations in functional activation and connectivity in language regions and networks of the brain that have been associated with AVH. The study found some evidence of altered activation in language-related areas of the brain associated with AVH in those without psychiatric diagnosis who have experienced childhood trauma, although this difference may be explained by participants' negative affective state. However, it did find evidence to suggest that those who have experienced childhood trauma display reduced functional connectivity in these areas compared to those who have not. Additionally, subtypes of childhood trauma were differentially associated with reduced functional connectivity, indicating that childhood trauma subtypes may be differentially related to neural alterations. These findings could be tentatively suggestive of neural mechanisms associated with risk for the development of AVH following childhood trauma. However, psychosis-like symptoms were not associated with a reduction in functional connectivity, so it is unclear whether these alterations in functional connectivity are related to AVH. This preliminary evidence suggests that further research in this area could be fruitful to advance

understanding of how childhood trauma may affect brain development to increase the risk of AVH.

Chapter IV: Integration, Impact and Dissemination

Overview

The aim of the final chapter of this project is to first summarise the integration of the systematic review and the empirical study which, although distinct, are interconnected research components. Then, it will provide an overview of the potential real-world implications and impact of this project's findings on academic beneficiaries and non-academic beneficiaries such as researchers, the general population, service users, clinicians, services and policy makers. Finally, the plans for dissemination of the review and research findings will be outlined.

Integration

Synergy between the systematic review and the empirical study

The overarching interest of the current project was the relationship between childhood trauma and auditory verbal hallucinations (AVH) in adulthood. Although the aims and methodologies employed by the different chapters of the current project were distinct, they were also interconnected. Namely, the systematic review explored the association between childhood trauma and AVH and the empirical study investigated potential neural mechanisms through which childhood trauma may increase the risk of AVH. Therefore, the overall aim of the project was to gain a better understanding of the relationship between childhood trauma and AVH.

Both chapters explored the relationship between childhood trauma and AVH. As the systematic review and the empirical study were conducted concurrently and due to the fMRI study having already been designed and the data largely collected, the systematic review was

not able to inform the design of the study. However, the clear and consistent findings from previous research of the significant association between childhood trauma and AVH highlighted in the systematic review provided a firm theoretical basis to explore the possible mechanisms of this relationship. Although evidence for the relationship between childhood trauma and AVH is abundant, causal claims cannot be made due to the overwhelming use of cross-sectional designs. However, this relationship meets some of the Bradford Hill Criteria (Hill, 1965), which consists of nine criteria to establish whether epidemiological, observational associations are causal. For example, the evidence for the existence of this relationship was shown to be consistent, with some evidence for a dose-response relationship found and confounds were controlled for in some studies which makes it more likely for the relationship to be specific. However, an important criterion is plausibility, which refers to the identification of plausible mechanisms which are likely to explain the association between the risk factor being studied and the outcome, which has not yet been clearly demonstrated. Therefore, there was an evident need identified for mechanisms of this relationship to be explored. Consequently, the empirical study sought to explore the possible neural mechanisms through which childhood trauma increases the risk of auditory hallucinations in adulthood and identifying mechanisms could provide further evidence to ascertain whether this relationship is causal.

Both chapters also investigated whether childhood trauma subtypes were differentially associated with AVH. This decision was made due to previous studies finding different relationships between symptoms of psychosis and subtypes of childhood trauma (Alameda et al., 2021; Bailey et al., 2018). Thus, it was deemed important for both the systematic review and the empirical study to investigate the relationships between not only combined childhood trauma, but also separate subtypes. Whilst the systematic review determined that most

childhood trauma subtypes were associated with AVH, the empirical study found that specific subtypes were associated with functional connectivity between two areas of the brain implicated in AVH; namely childhood sexual and physical abuse and emotional neglect.

Although the two chapters are interconnected, there are some fundamental differences. There were differences in the research questions and aims of the two chapters, with the systematic review focusing on studies that employed a different design to the empirical study. The systematic review identified studies looking at relationships between the two interested variables, whereas the empirical study was a functional Magnetic Resonance Imaging (fMRI) analysis using an experimental design. A review of neuroimaging studies focusing on AVH and childhood trauma was initially considered in order to identify existing research related to the empirical project. However, when initial literature searches were conducted, there was a lack of relevant studies identified and thus it was considered more appropriate to conduct the current review. Also, there was a difference in the populations being studied. Whereas the systematic review was focused on studies recruiting those who experience AVH, the fMRI project from which the data was analysed for the empirical study recruited a non-clinical sample. This was due to the empirical study being especially concerned with differences in brain function in those who have experienced childhood trauma but not gone on to develop mental health problems. This was because previous research highlighting that alterations in brain structure and function exist even in resilient individuals who have not gone on to develop mental health problems (Dannlowski et al., 2012; Teicher et al., 2016), thus indicating possible neural mechanisms for the development of mental health problems. Finally, the systematic review and empirical study differed in its conceptualisation of childhood trauma. Whilst the systematic review sought to include all possible types of childhood trauma including non-victimisation events, the empirical study used a well-known

valid and reliable measure of childhood trauma in the empirical study; the Childhood Trauma Questionnaire (Bernstein et al., 2003), which measures only childhood abuse and neglect. However, as the systematic review found little evidence for non-victimisation events being significantly associated with AVH, it is unlikely that the inclusion of a measure of non-victimisation events would have been useful.

Reflections on the study design

As the empirical study was an analysis of data from a wider fMRI project, the author did not have input into the design of the study. The hypotheses were developed by the author based on the previous childhood trauma neuroimaging literature, which found differences in brain structure, function and connectivity in areas of the brain associated with mental health problems (Paquola et al., 2016; Teicher et al., 2016) and differences in structure in language-related areas of the brain (Choi et al., 2009; De Brito et al., 2013). However, it is important to consider the limitations of the study design in order for future research conducted in this area to consider methodological weaknesses and improve on the study design. A main limitation was the lack of a measure of AVH proneness. Although the empirical study measured general psychosis-like symptoms, which included AVH, it did not specifically measure AVH. Therefore, it was not possible to explore whether brain function in the language network, which are the areas of the brain implicated in AVH (Allen et al., 2008, 2012; Jardri et al., 2011) was associated specifically with AVH. Measuring AVH proneness would have also indicated whether the groups were experiencing AVH – as AVH are also experienced by a proportion of the general population – and whether AVH proneness was associated with childhood trauma in this sample. Also, the sample size was smaller than expected. Initially, the fMRI project sought to recruit sixty participants, with thirty in both the High and Low Childhood Trauma (CT) Groups. However, data collection was unable to take place at

various points during the data collection period due to the COVID-19 pandemic, which meant that it was not possible to collect the full dataset. Compounding this, some of the datasets were unusable in analyses within the empirical study due to data collection problems and individual differences in brain anatomy making them unsuitable for group analyses. Also, the author was unable to carry out a pre-study power calculation to inform the sample size of this study as data collection had proceeded prior to the authors involvement for the current thesis. A sensitivity analysis was conducted, however, which indicated that the study was only powered to detect large effects. Having a bigger sample would have likely improved the study's power to detect small to medium effects, leading to a decreased risk of a Type II error.

Service user involvement

A briefing by the National Institute of Health and Care Research (NIHR) define service user involvement as "research being carried out "with" or "by" members of the public rather than "to", "about" or "for" them" (NIHR, 2021). It suggests that involving service users can make research more ethical in several ways; by making research more relevant, improving the quality of research and providing a different perspective. Therefore, it is preferable for service users to be involved in all stages of research, from the design of the study to dissemination of the findings. As a non-clinical sample was recruited for the empirical study, which consisted of a student population, the user in this context is the student population. There was little opportunity for service-user involvement in the empirical study, which is a significant limitation of the current project. The empirical study involved analysis of data collected for a wider fMRI project which had already been designed, with data collection having already started. Therefore, it was not possible for the author to involve students in the design phase of the empirical study, or in the analysis, due to specialist analytical skills and

software being required for fMRI analysis. Therefore, the lay summary was co-produced with a student to ensure that it was sufficiently clear and comprehensible to be understood by a wider audience. This was particularly valuable for summarising the results of the empirical project, as fMRI research is not often accessible to a wider audience and thus the student provided helpful feedback and input which allowed the lay summary to become more accessible.

Impact

The Research Excellence Framework defines impact as "an effect on, change or benefit to the economy, society, culture, public policy or services, health, the environment or quality of life, beyond academia" (Research Excellence Framework, 2021). It is thus important to consider the wider impact and implications of the current project for different beneficiaries including researchers, but also other groups such as the general public, service users and clinicians as well as policy makers.

Academic beneficiaries

The current project offers a unique contribution to the childhood trauma and auditory verbal hallucination research base which is likely to be of interest to researchers within disciplines such as clinical psychology, neuroscience and psychiatry. It is the first study to find differences in language network function within those who have experienced childhood trauma without psychiatric diagnosis and thus reveals potential fruitful avenues for further research in this area. The findings support hypotheses that experiencing childhood trauma may change developmental trajectories of the brain making individuals more vulnerable to mental health problems and symptoms in adulthood (Teicher & Samson, 2016). Future research should first seek to replicate the study, addressing the methodological

considerations, in a variety of populations such as the general population, those at high risk for psychosis and those from non-white ethnic backgrounds.

If findings are replicated, this would provide a basis for further research focusing on identifying the mechanisms through which childhood trauma increases risk for psychosis and more specifically AVH on the psychological level as well as neural level. The empirical study investigated the neural mechanisms through which childhood trauma may increase the risk of AVH in adulthood and thus further research should seek to extend these findings. Longitudinal research would be helpful to track brain development in language networks of the brain in both those who have experienced childhood trauma and those who have not, with and without AVH. This would allow a better understanding of how brain function, structure and connectivity may vary, from exposure to childhood trauma to the development of or non-development of AVH in adulthood. This could then also identify any possible neural resilience mechanisms in other areas of the brain in those who have experienced childhood trauma but have not gone onto develop AVH, which could have important implications for the development of novel treatments.

Also, it would be helpful for further research into the psychological factors that mediate the relationship between childhood trauma and AVH to be carried out. Indeed, the systematic review identified that most of the research investigating mediators in this relationship have focused on post-traumatic processes and found that variables such as dissociation do mediate the relationship between childhood trauma and AVH. However, few studies conducted mediation analyses and some did find that other variables not obviously related to post-traumatic processes also mediated this relationship. Thus, researchers should seek to clarify which psychological variables do mediate this relationship in order to better understand the

processes through which childhood trauma may lead to AVH. This could also have implications in terms of the developments of new or adapted psychological treatments.

The findings of this project open new avenues for research focusing on treatments for AVH. For example, if findings are replicated brain regions that are altered in those who have experienced childhood trauma could be targeted in clinical trials to normalise brain function. Also, if neural resilience mechanisms are found in those who have experienced childhood trauma, but have not gone on to develop AVH, areas of the brain responsible for making a person more resilient to AVH could be targeted to increase compensatory brain mechanisms in those who experience AVH. In addition, the trialling of adapted psychological interventions for AVH targeting the possible trauma-related aspects of AVH could be conducted in groups of people who have experienced childhood trauma.

Finally, although the systematic review suggested that most subtypes of abuse were associated with AVH in adulthood, the empirical study found that certain types of childhood trauma may be more strongly associated with functional alterations within areas of the brain implicated in AVH. Also, the systematic review found evidence of a combined/ cumulative effect of childhood trauma. Thus, further research could seek to clarify these relationships by looking at the individual as well as the combined effects of childhood trauma subtypes.

Non-academic beneficiaries

General population

Increasing the knowledge and raising awareness of the link between childhood trauma and AVH in clinical and non-clinical populations as well as increasing understanding of the etiological mechanisms that lead to AVH within the general population could have benefits.

Firstly, the knowledge that both childhood trauma and AVH are experienced by non-clinical populations could have a normalising effect on healthy voice hearers, their families and communities by reducing stigma associated with hearing voices. Furthermore, explanations for the development of AVH could be destigmatising and could also lead to healthy voice hearers who have experienced childhood trauma to better understand the reasons why they may have developed voices. This could be perceived as validating and could lead to decreased self-stigma. Indeed, the public perception of voice hearing can be highly stigmatising, as it is commonly believed that all who hear voices have a mental health problem such as schizophrenia, compounded by the largely negative portrayal of schizophrenia and AVH within the media (Vilhauer, 2015), often portrayed as being associated with violent or homicidal behaviour (Owen, 2012). This could then be internalised by the voice hearer, leading to secrecy, isolation and distress and may result in increased need for clinical care (Vilhauer, 2017). Thus, positioning AVH as an understandable response to trauma may reduce stigma and lead people to seek earlier support and intervention for both the effects of traumatic experiences in childhood and AVH.

Service users, clinicians and services

Similarly to members of the general population, it is hoped that the findings of this project will have a normalising, destigmatising and validating influence on service users, both through the knowledge that childhood trauma and AVH are experienced by non-clinical populations and through insight into potential factors that may have contributed to the development of AVH. It is also hoped that clinicians could use the findings of the current project to keep in mind that people who experience AVH could have also experienced trauma in childhood. For example, it would be helpful when assessing those with AVH to ask specific questions about any childhood traumatic experiences that service users may have

endured and any resulting current or historic post-traumatic stress disorder (PTSD) symptoms or processes that may have resulted from these experiences. As previous research has found thematic links between AVH and past traumatic experiences (Corstens & Longden, 2013; Hardy et al., 2005; Reiff et al., 2012), clinicians could carefully enquire about any thematic links between their AVH and childhood traumatic experiences. This could then inform idiosyncratic psychological formulations to include these early experiences and any PTSD symptoms that may be present and how they may link to the experience of AVH.

Whist treatment interventions were not explored within this project, the findings do imply that a population of people that experience AVH may benefit from the tailoring of existing treatments for AVH. For example, for those whose AVH are thought to be linked to decontextualised trauma-related intrusions following formulation, treatments to include PTSD psychoeducation and/or trauma-focused interventions may be especially beneficial. For example, Cognitive Behavioural Therapy (CBT) techniques could be implemented including the reliving of the traumatic memories which seek to allow traumatic memories to be properly processed and contextualised in an effort to reduce trauma-related intrusions (Ehlers & Clark, 2000).

At a service level, findings support recommendations that mental health services for people with severe mental health problems should employ a trauma-informed approach (National Health Service (NHS), 2019). This would call for an organisational change in the ways in which services are set up and how staff relate to all service users; to see through a trauma-lens, moving from asking “what is wrong with you?” to “what happened to you?” (Sweeney et al., 2018). Making these changes on a service level could prevent re-traumatisation and aid recovery from mental health problems.

Policy makers

The current project provides evidence to suggest that there is a clear and significant association between childhood trauma and AVH in adulthood and findings indicate that people who have experienced childhood trauma have altered language network function, potentially indicating neural mechanisms for this association. Findings also suggest that there may be a dose-response effect with combined or cumulative experiences of childhood trauma being more strongly associated with AVH in adulthood. Although childhood trauma is a common experience, it is also preventable. Thus, these findings along with the plethora of other research suggesting that childhood trauma increases risk of a variety of mental health problems in adulthood has clear implications that preventing childhood trauma could lead to a decreased risk of mental health problems. Therefore, early identification of childhood trauma, earlier intervention and the provision of early mental health support may decrease the risk of the development of AVH in adulthood. This provides a clear rationale for policies at the organisational level to reflect the need for early identification and intervention. The UK Trauma Council call for a "radical shift towards prevention" (UK Trauma Council, 2020) and recommend that focusing on mitigating the effect of childhood trauma could reduce the development of mental health problems. Current policies exist to reflect this, such as the Scottish Government's plans to prevent adverse childhood experiences and support children and adults who have experienced childhood trauma, through creating trauma-informed and trauma-responsive services and workforces (Scottish Government, 2018). This included the Scottish government funding national trauma training for workforces such as Health and Social Care. However, there is a strong need for other governments to implement similar policies within social care, schools and health services and youth organisations.

Dissemination

To maximise the impact of the current research project, the findings will be disseminated to a variety of audiences. To date, the empirical study findings have been presented to trainee clinical psychologists and staff members within the Doctor of Clinical Psychology Course at the Royal Holloway University of London (RHUL). Both the systematic review and the empirical study will be prepared and submitted for publication in peer-reviewed academic journals. Journals such as *Clinical Psychology Review*, *Schizophrenia Research, Psychological Medicine* and *Neuroimage* will be targeted for the empirical study. These journals have an impact factor ranging from 4.56-12.79 and have previously published articles on topics such as AVH in clinical and non-clinical populations and on the relationship between childhood trauma and psychiatric symptoms. Manuscripts will be uploaded to ResearchGate to enable wider access to the findings of the systematic review and the empirical study. Additionally, the current thesis will be uploaded to the RHUL's research portal; *RHUL Pure*. Also, conferences will be targeted such as the Combined Universities Brain Imaging Centre (CUBIC) conference and perhaps the International Childhood Trauma Conference. Finally, opportunities to share findings with local peer support groups and mental health services will be pursued, such as sharing the lay summary of the thesis with local groups including the London Hearing Voices Network.

References

Aas, M., Andreassen, O. A., Aminoff, S. R., Færden, A., Romm, K. L., Nesvåg, R., Berg, A. O., Simonsen, C., Agartz, I., & Melle, I. (2016). A history of childhood trauma is associated with slower improvement rates: Findings from a one-year follow-up study of patients with a first-episode psychosis. *BMC Psychiatry*, *16*(1), 1-8. https://doi.org/10.1186/S12888-016-0827-4

Abajobir, A. A., Kisely, S., Scott, J. G., Williams, G., Clavarino, A., Strathearn, L., & Najman, J. M. (2017). Childhood maltreatment and young adulthood hallucinations, delusional experiences, and psychosis: A longitudinal study. *Schizophrenia Bulletin*, *43*(5), 1045-1055. https://doi.org/10.1093/schbul/sbw175

Achenbach, T. M. (1997). *Manual for the young adult behavior checklist and young adult self report.* University of Vermont Department of Psychiatry.

Akbey, Z. Y., Yildiz, M., & Gündüz, N. (2019). Is there any association between childhood traumatic experiences, dissociation and psychotic symptoms in schziophrenic patients? *Psychiatry Investigation*, *16*(5), 346. https://doi.org/10.30773/pi.2019.02.10.2

Alameda, L., Christy, A., Rodriguez, V., Salazar De Pablo, G., Thrush, M., Shen, Y., Alameda, B., Spinazzola, E., Iacoponi, E., Trotta, G., Carr, E., Ruiz Veguilla, M., Aas, M., Morgan, C., & Murray, R. M. (2021). Association between Specific Childhood Adversities and Symptom Dimensions in People with Psychosis: Systematic Review and Meta-Analysis. *Schizophrenia Bulletin*, *47*(4), 975–985. https://doi.org/10.1093/schbul/sbaa199

Allen, P., Larøi, F., McGuire, P. K., & Aleman, A. (2008). The hallucinating brain: A review of structural and functional neuroimaging studies of hallucinations. *Neuroscience and Biobehavioral Reviews 32*(1), 175-191. https://doi.org/10.1016/j.neubiorev.2007.07.012

Allen, P., Modinos, G., Hubl, D., Shields, G., Cachia, A., Jardri, R., Thomas, P., Woodward,

T., Shotbolt, P., Plaze, M., & Hoffman, R. (2012). Neuroimaging auditory hallucinations in schizophrenia: From neuroanatomy to neurochemistry and beyond. *Schizophrenia Bulletin*, *38*(4), 695-703. https://doi.org/10.1093/schbul/sbs066

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5.* (5th ed.). American Psychiatric Publishing.

Anda, R. F., Brown, D. W., Felitti, V. J., Bremner, J. D., Dube, S. R., & Giles, W. H. (2007). Adverse Childhood Experiences and Prescribed Psychotropic Medications in Adults. *American Journal of Preventive Medicine*, *32*(5), 389-394. https://doi.org/10.1016/j.amepre.2007.01.005

Andreasen, N. C. (1984). Scale for the Assessment of Positive Symptoms (SAPS). *The British Journal of Psychiatry. Supplement*, *0*(7), 1-21.

Andrew, E. M., Gray, N. S., & Snowden, R. J. (2008). The relationship between trauma and beliefs about hearing voices: A study of psychiatric and non-psychiatric voice hearers. *Psychological Medicine*, *38*(10), 1409-1417. https://doi.org/10.1017/S003329170700253X

Arrindell, W. A., & Engebretsen, A. A. (2000). Convergent Validity of the ShortEMBU and the Parental Bonding Instrument (PBI): Dutch Findings. *Clinical Psychology and Psychotherapy*, *7*(4), 262-266. https://doi.org/10.1002/1099-0879(200010)7:4<262::AID-CPP257>3.0.CO;2-9

Assaf, M., Calhoun, V. D., Kuzu, C. H., Kraut, M. A., Rivkin, P. R., Hart, J., & Pearlson, G. D. (2006). Neural correlates of the object-recall process in semantic memory. *Psychiatry Research*, *147*(2–3), 115–126. https://doi.org/10.1016/J.PSCYCHRESNS.2006.01.002

Bailey, T., Alvarez-Jimenez, M., Garcia-Sanchez, A. M., Hulbert, C., Barlow, E., & Bendall, S. (2018). Childhood Trauma Is Associated With Severity of Hallucinations and Delusions in Psychotic Disorders: A Systematic Review and Meta-Analysis.

Schizophrenia Bulletin, *44*(5), 1111–1122. https://doi.org/10.1093/SCHBUL/SBX161

Baldwin, J. R., Reuben, A., Newbury, J. B., & Danese, A. (2019). Agreement Between Prospective and Retrospective Measures of Childhood Maltreatment: A Systematic Review and Meta-analysis. *JAMA Psychiatry*, *76*(6), 584–593. https://doi.org/10.1001/JAMAPSYCHIATRY.2019.0097

Barkus, E. J., Stirling, J., Hopkins, R. S., & Lewis, S. (2006). Cannabis-induced psychosis-like experiences are associated with high schizotypy. *Psychopathology*, *39*(4), 175-178. https://doi.org/10.1159/000092678

Barnes, G. M., & Windle, M. (1987). Family factors in adolescent alcohol and drug abuse. *Pediatrician*, *14*(1–2), 13-18.

Bartholomew, K., & Horowitz, L. M. (1991). Attachment Styles Among Young Adults: A Test of a Four-Category Model. *Journal of Personality and Social Psychology*, *61*(2), 226. https://doi.org/10.1037/0022-3514.61.2.226

Bauer, S. M., Schanda, H., Karakula, H., Olajossy-Hilkesberger, L., Rudaleviciene, P., Okribelashvili, N., Chaudhry, H. R., Idemudia, S. E., Gscheider, S., Ritter, K., & Stompe, T. (2011). Culture and the prevalence of hallucinations in schizophrenia. *Comprehensive Psychiatry*, *52*(3), 319–325. https://doi.org/10.1016/J.COMPPSYCH.2010.06.008

Baumeister, D., Sedgwick, O., Howes, O., & Peters, E. (2017). Auditory verbal hallucinations and continuum models of psychosis: A systematic review of the healthy voice-hearer literature. *Clinical Psychology Review*, *51*, 125–141. https://doi.org/10.1016/J.CPR.2016.10.010

Beavan, V., Read, J., & Cartwright, C. (2011). The prevalence of voice-hearers in the general population: A literature review. *20*(3), 281–292. https://doi.org/10.3109/09638237.2011.562262

Begemann, M. J. H., Sommer, I. E., Brand, R. M., Oomen, P. P., Jongeneel, A., Berkhout, J., Molenaar, R. E., Wielage, N. N., Toh, W. L., Rossell, S. L., & Bell, I. H. (2021). Auditory verbal hallucinations and childhood trauma subtypes across the psychosis continuum: a cluster analysis. *Cognitive Neuropsychiatry*, *27*(2-3), 150-168. https://doi.org/10.1080/13546805.2021.1925235

Bell, V., Halligan, P. W., & Ellis, H. D. (2006). The Cardiff Anomalous Perceptions Scale (CAPS): A new validated measure of anomalous perceptual experience. *Schizophrenia Bulletin*, *32*(2), 366-377. https://doi.org/10.1093/schbul/sbj014

Bentall, R. (2006). Madness explained: Why we must reject the Kraepelinian paradigm and replace it with a 'complaint-orientated' approach to understanding mental illness. *Medical Hypotheses*, *66*(2), 220–233. https://doi.org/10.1016/J.MEHY.2005.09.026

Bentall, R. P., De Sousa, P., Varese, F., Wickham, S., Sitko, K., Haarmans, M., & Read, J. (2014). From adversity to psychosis: pathways and mechanisms from specific adversities to specific symptoms. *Social Psychiatry and Psychiatric Epidemiology 49:7*, *49*(7), 1011–1022. https://doi.org/10.1007/S00127-014-0914-0

Bentall, R. P., & Varese, F. (2012). A level playing field?: Are bio-genetic and psychosocial studies evaluated by the same standards? *Psychosis, 4*(3), 183–190. https://doi.org/10.1080/17522439.2012.729856

Berg, A. O., Aas, M., Larsson, S., Nerhus, M., Hauff, E., Andreassen, O. A., & Melle, I. (2015). Childhood trauma mediates the association between ethnic minority status and more severe hallucinations in psychotic disorder. *Psychological Medicine, 45*(1), 133-142. https://doi.org/10.1017/S0033291714001135

Bernstein, D., & Fink, L. (1998). Childhood Trauma Questionnaire: A Retrospective Self-report. *The Psychological corporation*. The Psychological Corporation.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., Stokes,

J., Handelsman, L., Medrano, M., Desmond, D., & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse & Neglect, 27*(2), 169–190. https://doi.org/10.1016/S0145-2134(02)00541-0

Berry, K., Barrowclough, C., & Wearden, A. (2008). Attachment theory: A framework for understanding symptoms and interpersonal relationships in psychosis. *Behaviour Research and Therapy, 46*(12), 1275-1282. https://doi.org/10.1016/j.brat.2008.08.009

Bijl, R. V., Van Zessen, G., Ravelli, A., De Rijk, C., & Langendoen, Y. (1998). The Netherlands Mental Health Survey and Incidence Study (NEMESIS): Objectives and design. *Social Psychiatry and Psychiatric Epidemiology*, *33*(12), 581-586. https://doi.org/10.1007/s001270050097

Binder, J. R., Desai, R. H., Graves, W. W., & Conant, L. L. (2009). Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cerebral Cortex, 19*(12), 2767-2796. https://doi.org/10.1093/cercor/bhp055

Birchwood, M., Meaden, A., Trower, P., Gilbert, P., & Plaistow, J. (2000). The power and omnipotence of voices: Subordination and entrapment by voices and significant others. *Psychological Medicine*, *30*(2), 337-344. https://doi.org/10.1017/S0033291799001828

Bloomfield, M. A. P., Chang, T., Woodl, M. J., Lyons, L. M., Cheng, Z., Bauer-Staeb, C., Hobbs, C., Bracke, S., Kennerley, H., Isham, L., Brewin, C., Billings, J., Greene, T., & Lewis, G. (2021). Psychological processes mediating the association between developmental trauma and specific psychotic symptoms in adults: a systematic review and meta-analysis. *World Psychiatry*, *20*(1), 107–123. https://doi.org/10.1002/WPS.20841

Bortolon, C., & Raffard, S. (2018). Dissociation Mediates the Relationship between Childhood Trauma and Experiences of Seeing Visions in a French Sample. *Journal of Nervous and Mental Disease, 206*(11), 850-858.

https://doi.org/10.1097/NMD.0000000000000885

Bortolon, C., Seillé, J., & Raffard, S. (2017). Exploration of trauma, dissociation, maladaptive schemas and auditory hallucinations in a French sample. *Cognitive Neuropsychiatry, 22*(6), 468-485. https://doi.org/10.1080/13546805.2017.1387524

Botvinick, M. M., Carter, C. S., Braver, T. S., Barch, D. M., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review, 108*(3), 624. https://doi.org/10.1037/0033-295X.108.3.624

Brand, R. M., Bendall, S., Hardy, A., Rossell, S. L., & Thomas, N. (2021). Trauma-focused imaginal exposure for auditory hallucinations: A case series. *Psychology and Psychotherapy, 94 (2*), 408–425. https://doi.org/10.1111/PAPT.12284

Bremner, J. D., Bolus, R., & Mayer, E. A. (2007). Psychometric properties of the early trauma inventory-self report. *Journal of Nervous and Mental Disease, 195*(3), 211. https://doi.org/10.1097/01.nmd.0000243824.84651.6c

Button, K. S., Ioannidis, J., Mokrysz, C., Nosek, B. A., Flint, J., Robinson, E. S., & Munafò, M. R. (2013). Power failure: why small sample size undermines the reliability of neuroscience. *Nature reviews neuroscience, 14*(5), 365-376.

Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience, 12*(1), 1-47. https://doi.org/10.1162/08989290051137585

Carlier, I. V. E., Lamberts, R. D., Van Uchelen, A. J., & Gersons, B. P. R. (1998). Clinical utility of a brief diagnostic test for posttraumatic stress disorder. *Psychosomatic Medicine, 60*(1), 42-47. https://doi.org/10.1097/00006842-199801000-00010

Castle, D. J., Jablensky, A., McGrath, J. J., Carr, V., Morgan, V., Waterreus, A., Valuri, G., Stain, H., McGuffin, P., & Farmer, A. (2006). The diagnostic interview for psychoses (DIP): Development, reliability and applications. *Psychological Medicine, 36*(1), 69-80.

https://doi.org/10.1017/S0033291705005969

Chadwick, P., Lees, S., & Birchwood, M. (2000). The revised beliefs about voices questionnaire (BAVQ-R). *British Journal of Psychiatry*, *177*(3), 229-232. https://doi.org/10.1192/bjp.177.3.229

Choi, J., Jeong, B., Rohan, M. L., Polcari, A. M., & Teicher, M. H. (2009). Preliminary Evidence for White Matter Tract Abnormalities in Young Adults Exposed to Parental Verbal Abuse. *Biological Psychiatry*, *65*(3), 227-234. https://doi.org/10.1016/j.biopsych.2008.06.022

Cole, J. D., & Kazarian, S. S. (1988). The level of expressed emotion scale: A new measure of expressed emotion. *Journal of Clinical Psychology, 44*(3), 392-397. https://doi.org/10.1002/1097-4679(198805)44:3<392::AID-JCLP2270440313>3.0.CO;2-3

Colman, I., Kingsbury, M., Garad, Y., Zeng, Y., Naicker, K., Patten, S., Jones, P. B., Wild, T. C., & Thompson, A. H. (2016). Consistency in adult reporting of adverse childhood experiences. *Psychological Medicine*, *46*(3), 543–549. https://doi.org/10.1017/S0033291715002032

Connor, C., & Birchwood, M. (2012). Abuse and dysfunctional affiliations in childhood: an exploration of their impact on voice-hearers' appraisals of power and expressed emotion. *Psychosis*, *4*(1), 19-31. https://doi.org/10.1080/17522439.2011.630745

Connor, K. M., & Davidson, J. R. T. (2003). Development of a new Resilience scale: The Connor-Davidson Resilience scale (CD-RISC). *Depression and Anxiety*, *18*(2), 76–82. https://doi.org/10.1002/DA.10113

Corstens, D., & Longden, E. (2013). The origins of voices: links between life history and voice hearing in a survey of 100 cases. *Psychosis*, *5*(3), 270–285. https://doi.org/10.1080/17522439.2013.816337

Cristofaro, S. L., Cleary, S. D., Ramsay Wan, C., Broussard, B., Chapman, C., Haggard, P. J., Jananeh, S., Myers, N. L., & Compton, M. T. (2013). Measuring trauma and stressful events in childhood and adolescence among patients with first-episode psychosis: Initial factor structure, reliability, and validity of the trauma experiences checklist. *Psychiatry Research*, *210*(2), 618-625. https://doi.org/10.1016/j.psychres.2013.06.015

Ćurčić-Blake, B., Ford, J. M., Hubl, D., Orlov, N. D., Sommer, I. E., Waters, F., Allen, P., Jardri, R., Woodruff, P. W., David, O., Mulert, C., Woodward, T. S., & Aleman, A. (2017). Interaction of language, auditory and memory brain networks in auditory verbal hallucinations. *Progress in Neurobiology*, *148*, 1-20. https://doi.org/10.1016/j.pneurobio.2016.11.002

Daalman, K., Diederen, K. M. J., Derks, E. M., van Lutterveld, R., Kahn, R. S., & Sommer, I. E. C. (2012). Childhood trauma and auditory verbal hallucinations. *Psychological Medicine*, *42*, 2475–2484.

Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd, D., Domschke, K., Hohoff, C., Ohrmann, P., Bauer, J., Lindner, C., Postert, C., Konrad, C., Arolt, V., Heindel, W., Suslow, T., & Kugel, H. (2012). Limbic scars: Long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. *Biological Psychiatry*, *71*(4), 286-293. https://doi.org/10.1016/j.biopsych.2011.10.021

Darves-Bornoz, J. M., Degiovanni, A., & Gaillard, P. (1999). Validation of a French version of the Dissociative Experiences Scale in a rape-victim population. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie*, *44*(3), 271–275. https://doi.org/10.1177/070674379904400308

Davidson, J., & Smith, R. (1990). Traumatic experiences in psychiatric outpatients. *Journal of Traumatic Stress*, *3*(3), 459-475. https://doi.org/10.1007/BF00974785

De Bellis, M. D., Keshavan, M. S., Shifflett, H., Iyengar, S., Beers, S. R., Hall, J., & Moritz, G. (2002). Brain structures in pediatric maltreatment-related posttraumatic stress disorder: A sociodemographically matched study. *Biological Psychiatry*, *52*(11), 1066-1078. https://doi.org/10.1016/S0006-3223(02)01459-2

De Brito, S. A., Viding, E., Sebastian, C. L., Kelly, P. A., Mechelli, A., Maris, H., & McCrory, E. J. (2013). Reduced orbitofrontal and temporal grey matter in a community sample of maltreated children. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *54*(1), 105-112. https://doi.org/10.1111/j.1469-7610.2012.02597.x

Del Re, E. C., Stone, W. S., Bouix, S., Seitz, J., Zeng, V., Guliano, A., Somes, N., Zhang, T., Reid, B., Lyall, A., Lyons, M., Li, H., Whitfield-Gabrieli, S., Keshavan, M., Seidman, L. J., McCarley, R. W., Wang, J., Tang, Y., Shenton, M. E., & Niznikiewicz, M. A. (2021). Baseline Cortical Thickness Reductions in Clinical High Risk for Psychosis: Brain Regions Associated with Conversion to Psychosis Versus Non-Conversion as Assessed at One-Year Follow-Up in the Shanghai-At-Risk-for-Psychosis (SHARP) Study. *Schizophrenia Bulletin*, *47*(2), 562-574. https://doi.org/10.1093/schbul/sbaa127

Derogatis, L. R., & Melisaratos, N. (1983). The Brief Symptom Inventory: an introductory report. *Psychological Medicine*, *13*(3), 595–605. https://doi.org/10.1017/S0033291700048017

Deschamps, I., Baum, S. R., & Gracco, V. L. (2014). On the role of the supramarginal gyrus in phonological processing and verbal working memory: Evidence from rTMS studies. *Neuropsychologia*, *53*(1), 39-46. https://doi.org/10.1016/j.neuropsychologia.2013.10.015

Diederen, K. M. J., Daalman, K., De Weijer, A. D., Neggers, S. F. W., Van Gastel, W., Blom, J. D., Kahn, R. S., & Sommer, I. E. C. (2012). Auditory hallucinations elicit similar brain activation in psychotic and nonpsychotic individuals. *Schizophrenia*

Bulletin, *38*(5), 1074-1082. https://doi.org/10.1093/schbul/sbr033

Dillon, D. G., Holmes, A. J., Birk, J. L., Brooks, N., Lyons-Ruth, K., & Pizzagalli, D. A. (2009). Childhood Adversity Is Associated with Left Basal Ganglia Dysfunction During Reward Anticipation in Adulthood. *Biological Psychiatry*, *66*(3), 206-213. https://doi.org/10.1016/j.biopsych.2009.02.019

Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy*, *38*(4), 319–345. https://doi.org/10.1016/S0005-7967(99)00123-0

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences of the United States of America*, *113*(28), 7900–7905. https://doi.org/10.1073/PNAS.1602413113/SUPPL_FILE/PNAS.1602413113.SAPP.PDF

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & Marks, J. S. (2019). Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, *56*(6), 245-258. https://doi.org/10.1016/j.amepre.2019.04.001

Foa, E. B., Cashman, L., Jaycox, L., & Perry, K. (1997). The validation of a self-report measure of posttraumatic stress disorder: The posttraumatic diagnostic scale. *Psychological Assessment*, *9*(4), 445. https://doi.org/10.1037/1040-3590.9.4.445

Freeman, D. (2007). Suspicious minds: the psychology of persecutory delusions. *Clinical Psychology Review*, *27*(4), 425–457. https://doi.org/10.1016/J.CPR.2006.10.004

Freeman, D., & Fowler, D. (2009). Routes to psychotic symptoms: Trauma, anxiety and psychosis-like experiences. *Psychiatry Research*, *169*(2), 107-112.

https://doi.org/10.1016/j.psychres.2008.07.009

Galletti, C., Paolini, E., Tortorella, A., & Compton, M. T. (2017). Auditory and non-auditory hallucinations in first-episode psychosis: Differential associations with diverse clinical features. *Psychiatry Research, 254*, 268-274. https://doi.org/10.1016/j.psychres.2017.04.056

Ge, X., Conger, R. D., Lorenz, F. O., & Simons, R. L. (1994). Parents' stressful life events and adolescent depressed mood. *Journal of Health and Social Behavior*, *35*(1), 28-44. https://doi.org/10.2307/2137333

Gicas, K. M., Parmar, P. K., Fabiano, G. F., & Mashhadi, F. (2022). Substance-induced psychosis and cognitive functioning: A systematic review. *Psychiatry Research*, *308*, 114361. https://doi.org/10.1016/J.PSYCHRES.2021.114361

Goldberg, L. R., & Freyd, J. J. (2006). Self-reports of potentially traumatic experiences in an adult community sample: Gender differences and test-retest stabilities of the items in a brief betrayal-trauma survey. *Journal of Trauma and Dissociation*, *7*(3), 39-63. https://doi.org/10.1300/J229v07n03_04

Goldstone, E., Farhall, J., & Ong, B. (2012). Modelling the emergence of hallucinations: Early acquired vulnerabilities, proximal life stressors and maladaptive psychological processes. *Social Psychiatry and Psychiatric Epidemiology, 47*(9), 1367-1380. https://doi.org/10.1007/s00127-011-0446-9

Gómez, J. M., Kaehler, L. A., & Freyd, J. J. (2014). Are hallucinations related to betrayal trauma exposure? A three-study exploration. *Psychological Trauma: Theory, Research, Practice, and Policy*, *6*(6), 675. https://doi.org/10.1037/a0037084

Grodzinsky, Y., & Amunts, K. (2006). *Broca's Region*. Oxford University Press.

Haddaway, N. R., Pritchard, C. C., & McGuinness, L. A. (2021). *PRISMA2020: R package and ShinyApp for producing PRISMA 2020 compliant flow diagrams.* Zenodo.

Haddock, G., McCarron, J., Tarrier, N., & Faragher, E. B. (1999). Scales to measure dimensions of hallucinations and delusions: The psychotic symptom rating scales (PSYRATS). *Psychological Medicine*, *29*(4), 879-889. https://doi.org/10.1017/S0033291799008661

Hanson, J. L., Albert, D., Iselin, A. M. R., Carré, J. M., Dodge, K. A., & Hariri, A. R. (2016). Cumulative stress in childhood is associated with blunted reward-related brain activity in adulthood. *Social Cognitive and Affective Neuroscience*, *11*(3), 405-412. https://doi.org/10.1093/scan/nsv124

Hardy, A., Emsley, R., Freeman, D., Bebbington, P., Garety, P. A., Kuipers, E. E., Dunn, G., & Fowler, D. (2016). Psychological Mechanisms Mediating Effects between Trauma and Psychotic Symptoms: The Role of Affect Regulation, Intrusive Trauma Memory, Beliefs, and Depression. *Schizophrenia Bulletin*, *42, S34-S43*. https://doi.org/10.1093/schbul/sbv175

Hardy, A., Fowler, D., Freeman, D., Smith, B., Steel, C., Evans, J., Garety, P., Kuipers, E., Bebbington, P., & Dunn, G. (2005). Trauma and hallucinatory experience in psychosis. *Journal of Nervous and Mental Disease*, *193*(8), 501–507. https://doi.org/10.1097/01.NMD.0000172480.56308.21

Harmon-Jones, E., & Beer, J. S. (2009). *Methods in social neuroscience.* Guildford Press.

Hayes, A. F. (2018). *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach* (2nd ed.). The Guilford Press.

Hayward, M., Denney, J., Vaughan, S., & Fowler, D. (2008). The voice and you: Development and psychometric evaluation of a measure of relationships with voices. *Clinical Psychology and Psychotherapy*, *15*(1), 45-52. https://doi.org/10.1002/cpp.561

Healy, C., Brannigan, R., Dooley, N., Coughlan, H., Clarke, M., Kelleher, I., & Cannon, M. (2019). Childhood and adolescent psychotic experiences and risk of mental disorder: a

systematic review and meta-analysis. *Psychological Medicine*, *49*(10), 1589–1599. https://doi.org/10.1017/S0033291719000485

Henrich, J., Heine, S. J., & Norenzayan, A. (2010). The weirdest people in the world? *Behavioral and Brain Sciences*, *33*(2-3), 61-83. https://doi.org/10.1017/S0140525X0999152X

Hill, A. B. (1965). The environment and disease: association or causation? *Journal of the Royal Society of Medicine*, *108*(1), 32–37. https://doi.org/10.1177/0141076814562718

Horowitz, M., Wilner, N., & Alvarez, W. (1979). Impact of event scale: A measure of subjective stress. *Psychosomatic Medicine*, *41*(3), 209-218. https://doi.org/10.1097/00006842-197905000-00004

Jacobs, J., Agho, K., Stevens, G., & Raphael, B. (2012). Do childhood adversities cluster in predictable ways? A systematic review. *Vulnerable Children and Youth Studies*, *7*(2), 103–115. https://doi.org/10.1080/17450128.2012.658886

Jardri, R., Pouchet, A., Pins, D., & Thomas, P. (2011). Cortical activations during auditory verbal hallucinations in schizophrenia: A coordinate-based meta-analysis. *American Journal of Psychiatry*, *168*(1), 73-81. https://doi.org/10.1176/appi.ajp.2010.09101522

Jastak, J., & Wilkinson, G. S. (1984). *Wide range achievement test: Revised edition.* Jastak Associates Inc.

Johns, L. C., & Van Os, J. (2001). The continuity of psychotic experiences in the general population. *Clinical Psychology Review*, *21*(8), 1125–1141. https://doi.org/10.1016/S0272-7358(01)00103-9

Jonides, J., Schumacher, E. H., Smith, E. E., Koeppe, R. A., Awh, E., Reuter-Lorenz, P. A., Marshuetz, C., & Willis, C. R. (1998). The role of parietal cortex in verbal working memory. *Journal of Neuroscience*, *18*(13), 5026-5034. https://doi.org/10.1523/jneurosci.18-13-05026.1998

Kart, A., & Türkçapar, H. (2019). The effects of childhood emotional abuse on aggressive obsessions among patients with obsessive compulsive disorder may be mediated by symptoms of depression and anxiety. *Psychiatry and Clinical Psychopharmacology*, *29*(4), 411-417.

Kay, S. R., Flszbeln, A., & Qpjer, L. A. (1967). The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261-276.

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., Aguilar-Gaxiola, S., Alhamzawi, A. O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., De Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O. & Williams, D. R. (2010). Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry*, *197*(5), 378–385. https://doi.org/10.1192/BJP.BP.110.080499

Kessler, R. C., & Üstün, B. B. (2004). The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *International Journal of Methods in Psychiatric Research*, *13*(2), 93-121. https://doi.org/10.1002/mpr.168

Kim, H., Kim, D., & Kim, S. H. (2018). Association of types of delusions and hallucinations with childhood abuse and neglect among inpatients with schizophrenia in South Korea: A preliminary study. *Psychosis*, *10*(3), 208–212. https://doi.org/10.1080/17522439.2018.1472627

Kingdon, D. G., Ashcroft, K., Bhandari, B., Gleeson, S., Warikoo, N., Symons, M., Taylor, L., Lucas, E., Mahendra, R., Ghosh, S., Mason, A., Badrakalimuthu, R., Hepworth, C., Read, J., & Mehta, R. (2010). Schizophrenia and borderline personality disorder: similarities and differences in the experience of auditory hallucinations, paranoia, and childhood trauma. *The Journal of Nervous and Mental Disease*, *198*(6), 399–403.

https://doi.org/10.1097/NMD.0B013E3181E08C27

Knight, R. A., & Silverstein, S. M. (2001). A process-oriented approach for averting confounds resulting from general performance deficiencies in schizophrenia. *Journal of Abnormal Psychology, 110*(1), 15. https://doi.org/10.1037/0021-843X.110.1.15

Kohn, P. M., & Macdonald, J. E. (1992). The Survey of Recent Life Experiences: A decontaminated hassles scale for adults. *Journal of Behavioral Medicine, 15*(2), 221-236. https://doi.org/10.1007/BF00848327

Köse, G., Jessen, K., Ebdrup, B. H., & Nielsen, M. Ø. (2018). Associations between cortical thickness and auditory verbal hallucinations in patients with schizophrenia: A systematic review. *Psychiatry Research - Neuroimaging, 282*, 31-39. https://doi.org/10.1016/j.pscychresns.2018.10.005

Kraut, M. A., Kremen, S., Segal, J. B., Calhoun, V., Moo, L. R., & Hart, J. (2002). Object activation from features in the semantic system. *Journal of Cognitive Neuroscience, 14*(1), 24-36. https://doi.org/10.1162/089892902317205294

Lee, S. H., Park, Y., Jin, M. J., Lee, Y. J., & Hahn, S. W. (2017). Childhood trauma associated with enhanced high frequency band powers and induced subjective inattention of adults. *Frontiers in behavioral neuroscience, 11*, 148.

Lemons, C. J. (2009). Replication of significant correlations in small samples. *Evaluation & research in education, 22*(2-4), 75-86.

Larøi, F. (2012). How do auditory verbal hallucinations in patients differ from those in non-patients? *Frontiers in Human Neuroscience, 6*, 25. https://doi.org/10.3389/FNHUM.2012.00025

Larøi, F., Sommer, I. E., Blom, J. D., Fernyhough, C., Ffytche, D. H., Hugdahl, K., Johns, L. C., McCarthy-Jones, S., Preti, A., Raballo, A., Slotema, C. W., Stephane, M., & Waters, F. (2012). The Characteristic Features of Auditory Verbal Hallucinations in Clinical and

Nonclinical Groups: State-of-the-Art Overview and Future Directions. *Schizophrenia Bulletin*, *38*(4), 724–733. https://doi.org/10.1093/SCHBUL/SBS061

Launay, G., & Slade, P. (1981). The measurement of hallucinatory predisposition in male and female prisoners. *Personality and Individual Differences*, *2*(3), 221-234. https://doi.org/10.1016/0191-8869(81)90027-1

Lenhard, W., & Lenhard, A. (2017). *Computation of Effect Sizes.* Psychometrica. DOI: 10.13140/RG.2.1.3478.4245

Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy*, *33*(3), 335–343. https://doi.org/10.1016/0005-7967(94)00075-U

Mason, O. J., Brett, E., Collinge, M., Curr, H., & Rhodes, J. (2009). Childhood abuse and the content of delusions. *Child Abuse and Neglect*, *33*(4), 205-208. https://doi.org/10.1016/j.chiabu.2008.07.003

Matheson, S. L., Shepherd, A. M., Pinchbeck, R. M., Laurens, K. R., & Carr, V. J. (2013). Childhood adversity in schizophrenia: A systematic meta-analysis. *Psychological Medicine*, *43*(2), 225-238. https://doi.org/10.1017/S0033291712000785

McCarthy-Jones, S. (2011). Voices from the storm: A critical review of quantitative studies of auditory verbal hallucinations and childhood sexual abuse. *Clinical Psychology Review*, *31*(6), 983–992. https://doi.org/10.1016/J.CPR.2011.05.004

McCarthy-Jones, S., & Fernyhough, C. (2011). The varieties of inner speech: Links between quality of inner speech and psychopathological variables in a sample of young adults. *Consciousness and Cognition*, *20*(4), 1586-1593. https://doi.org/10.1016/j.concog.2011.08.005

McGuffin, P., Farmer, A., & Harvey, I. (1991). A polydiagnostic application of operational

criteria in studies of psychotic illness: Development and reliability of the OPCRIT system. *Archives of General Psychiatry*, *48*(8), 764-770. https://doi.org/10.1001/archpsyc.1991.01810320088015

McHugo, G. J., Caspi, Y., Kammerer, N., Mazelis, R., Jackson, E. W., Russell, L., Clark, C., Liebschutz, J., & Kimerling, R. (2005). The assessment of trauma history in women with co-occurring substance abuse and mental disorders and a history of interpersonal violence. *Journal of Behavioral Health Services and Research*, *32*(2), 113-127. https://doi.org/10.1007/BF02287261

McKay, M. T., Cannon, M., Chambers, D., Conroy, R. M., Coughlan, H., Dodd, P., Healy, C., O'Donnell, L., & Clarke, M. C. (2021). Childhood trauma and adult mental disorder: A systematic review and meta-analysis of longitudinal cohort studies. *Acta Psychiatrica Scandinavica*, *143*(3), 189–205. https://doi.org/10.1111/ACPS.13268

Misiak, B., Moustafa, A. A., Kiejna, A., & Frydecka, D. (2016). Childhood traumatic events and types of auditory verbal hallucinations in first-episode schizophrenia patients. *Comprehensive Psychiatry*, *66,* 17-22. https://doi.org/10.1016/j.comppsych.2015.12.003

Modinos, G., Costafreda, S. G., Van Tol, M. J., McGuire, P. K., Aleman, A., & Allen, P. (2013). Neuroanatomy of auditory verbal hallucinations in schizophrenia: A quantitative meta-analysis of voxel-based morphometry studies. *Cortex*, *49*(4), 1046-1055. https://doi.org/10.1016/j.cortex.2012.01.009

Mohammadzadeh, A., Azadi, S., King, S., Khosravani, V., & Sharifi Bastan, F. (2019). Childhood trauma and the likelihood of increased suicidal risk in schizophrenia. *Psychiatry Research*, *275*, 100–107. https://doi.org/10.1016/J.PSYCHRES.2019.03.023

Morgenroth, E., Saviola, F., Gilleen, J., Allen, B., Lührs, M., W. Eysenck, M., & Allen, P. (2020). Using connectivity-based real-time fMRI neurofeedback to modulate attentional and resting state networks in people with high trait anxiety. *NeuroImage: Clinical*, *25*,

102191. https://doi.org/10.1016/J.NICL.2020.102191

Morrison, A. P., Renton, J. C., Dunn, H., Williams, S., & Bentall, R. P. (2004). Cognitive therapy for psychosis: A formulation-based approach. *Cognitive Therapy for Psychosis: A Formulation-Based Approach*. Routledge.

Mrug, S., Loosier, P. S., & Windle, M. (2008). Violence Exposure Across Multiple Contexts: Individual and Joint Effects on Adjustment. *American Journal of Orthopsychiatry*, *78*(1), 70-84. https://doi.org/10.1037/0002-9432.78.1.70

Mrug, S., Madan, A., & Windle, M. (2012). Temperament alters susceptibility to negative peer influence in early adolescence. *Journal of Abnormal Child Psychology, 40*(2), 201-209. https://doi.org/10.1007/s10802-011-9550-2

Mueller, M., D'Addario, M., Egger, M., Cevallos, M., Dekkers, O., Mugglin, C., & Scott, P. (2018). Methods to systematically review and meta-analyse observational studies: A systematic scoping review of recommendations. *BMC Medical Research Methodology, 18*(1), 1-18. https://doi.org/10.1186/s12874-018-0495-9

Mueller, S., Wang, D., Fox, M. D., Yeo, B. T., Sepulcre, J., Sabuncu, M. R., Shafee, R., Lu, J. & Liu, H. (2013). Individual variability in functional connectivity architecture of the human brain. *Neuron, 77*(3), 586-595.

Nathou, C., Etard, O., & Dollfus, S. (2019). Auditory verbal hallucinations in schizophrenia: current perspectives in brain stimulation treatments. *Neuropsychiatric Disease and Treatment, 15*, 2105. https://doi.org/10.2147/NDT.S168801

National Heart Lung and Blood Institute (NHLBI). (2014). *Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies*. National Institutes of Health, Department of Health and Human Services.

National Institute for Health and Care Excellence (NICE). (2014, March 01). *Psychosis and schizophrenia in adults: prevention and management*. NICE.

https://www.nice.org.uk/guidance/CG178

National Institute for Health and Care Research (NIHR). (2021, April 05). *Briefing notes for researchers - public involvement in NHS, health and social care research.* NIHR. Https://Www.Nihr.Ac.Uk/Documents/Briefing-Notes-for-Researchers-Public-Involvement-in-Nhs-Health-and-Social-Care-Research/27371.

Nayani, T. H., & David, A. S. (1996). The auditory hallucination: A phenomenological survey. *Psychological Medicine, 26*(1), 177–189. https://doi.org/10.1017/s003329170003381x

NHS. (2019, August 21). *NHS Long Term Plan*. NHS. https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/

O'Reilly, J. X., Woolrich, M. W., Behrens, T. E. J., Smith, S. M., & Johansen-Berg, H. (2012). Tools of the trade: Psychophysiological interactions and functional connectivity. *Social Cognitive and Affective Neuroscience, 7*(5). https://doi.org/10.1093/scan/nss055

Offen, L., Waller, G., & Thomas, G. (2003). Is reported childhood sexual abuse associated with the psychopathological characteristics of patients who experience auditory hallucinations? *Child Abuse and Neglect, 27*(8), 919-927. https://doi.org/10.1016/S0145-2134(03)00139-X

Owen, P. R. (2012). Portrayals of Schizophrenia by Entertainment Media: A Content Analysis of Contemporary Movies. *Psychiatric Services, 63*(7), 655–659. https://doi.org/10.1176/APPI.PS.201100371

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S. & Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *International Journal of Surgery, 88,* 105906.

https://doi.org/10.1136/bmj.n71

Paquola, C., Bennett, M. R., & Lagopoulos, J. (2016). Understanding heterogeneity in grey matter research of adults with childhood maltreatment—A meta-analysis and review. *Neuroscience & Biobehavioral Reviews*, *69*, 299–312. https://doi.org/10.1016/J.NEUBIOREV.2016.08.011

Pearce, J., Simpson, J., Berry, K., Bucci, S., Moskowitz, A., & Varese, F. (2017). Attachment and dissociation as mediators of the link between childhood trauma and psychotic experiences. *Clinical Psychology and Psychotherapy*, *24*(6), 1304-1312. https://doi.org/10.1002/cpp.2100

Perona-Garcelán, S., Carrascoso- López, F., García-Montes, J. M., Ductor-Recuerda, M. J., López Jiménez, A. M., Vallina-Fernández, O., Pérez-Álvarez, M., & Gómez-Gómez, M. T. (2012). Dissociative experiences as mediators between childhood trauma and auditory hallucinations. *Journal of Traumatic Stress*, *25*(3), 323-329. https://doi.org/10.1002/jts.21693

Perona-Garcelán, S., García-Montes, J. M., Cuevas-Yust, C., Pérez-Álvarez, M., Ductor-Recuerda, M. J., Salas-Azcona, R., & Gómez-Gómez, M. T. (2010). A preliminary exploration of trauma, dissociation, and positive psychotic symptoms in a spanish sample. *Journal of Trauma and Dissociation, 11*(3), 284-292. https://doi.org/10.1080/15299731003786462

Poldrack, R. A., Baker, C. I., Durnez, J., Gorgolewski, K. J., Matthews, P. M., Munafò, M. R., Nichols, T. E., Poline, J. B., Vul, E., & Yarkoni, T. (2017). Scanning the horizon: Towards transparent and reproducible neuroimaging research. *Nature Reviews Neuroscience, 18*(2), 115-126. https://doi.org/10.1038/nrn.2016.167

Poldrack, R. A., Nichols, T., & Mumford, J. (2011). Handbook of Functional MRI Data Analysis. *Handbook of Functional MRI Data Analysis*. Cambridge University Press.

Preacher, K. J. (2015). Extreme groups designs. In Cautin, R.L., & Lilienfeld, S.O. (Eds.), *The encyclopedia of clinical psychology* (pp.1189-1192). John Wiley & Sons Inc.

Price, C. J. (2010). The anatomy of language: A review of 100 fMRI studies published in 2009. *Annals of the New York Academy of Sciences*, *1191*(1), 62-88. https://doi.org/10.1111/j.1749-6632.2010.05444.x

Prokopez, C. R., Cesoni, O. M., Caporusso, G. B., Reffino-Pereyra, M. L., Alberio, G., & Vallejos, M. (2018). Prevalence and clinical impact of childhood adversities in women with schizophrenia. *Clinical Schizophrenia & Related Psychoses*. https://doi.org/10.3371/csrp.prce.061518

Prokopez, C. R., Vallejos, M., Farinola, R., Alberio, G., Caporusso, G. B., Cozzarin, L. G., Chiapella, L. C., Fuentes, P., & Daray, F. M. (2020). The history of multiple adverse childhood experiences in patients with schizophrenia is associated with more severe symptomatology and suicidal behavior with gender-specific characteristics. *Psychiatry Research*, *293*, 113411. https://doi.org/10.1016/j.psychres.2020.113411

Rajkumar, R. P. (2015). The Impact of Childhood Adversity on the Clinical Features of Schizophrenia. *Schizophrenia Research and Treatment*, *2015*. https://doi.org/10.1155/2015/532082

Ratcliff, K., Farhall, J., & Shawyer, F. (2011). Auditory hallucinations: a review of assessment tools. *Clinical Psychology & Psychotherapy*, *18*(6), 524–534. https://doi.org/10.1002/CPP.729

Read, J., Harper, D., & Kennedy, A. (n.d.). Do adult mental health services identify child abuse and neglect? A systematic review. *International Journal of Mental Health Nursing*, *27*, 7–19. https://doi.org/10.1111/inm.12369

Reiff, M., Castille, D. M., Muenzenmaier, K., & Link, B. (2012). Childhood abuse and the content of adult psychotic symptoms. *Psychological Trauma: Theory, Research,*

Practice, and Policy, *4*(4), 356–369. https://doi.org/10.1037/A0024203

Research Excellence Framework. (2022, May 12). *Detailed guidance on the REF 2021 results.* REF2021. Https://Ref.Ac.Uk/Guidance-on-Results/Guidance-on-Ref-2021-Results/.

Rosen, C., McCarthy-Jones, S., Chase, K. A., Jones, N., Luther, L., Melbourne, J. K., Sudhalkar, N., & Sharma, R. P. (2020). The role of inner speech on the association between childhood adversity and 'hearing voices.' *Psychiatry Research*, *286*, 112866. https://doi.org/10.1016/j.psychres.2020.112866

Rosen, C., McCarthy-Jones, S., Jones, N., Chase, K. A., & Sharma, R. P. (2018). Negative voice-content as a full mediator of a relation between childhood adversity and distress ensuing from hearing voices. *Schizophrenia Research*, *199*, 361-366. https://doi.org/10.1016/j.schres.2018.03.030

Samplin, E., Ikuta, T., Malhotra, A. K., Szeszko, P. R., & DeRosse, P. (2013). Sex differences in resilience to childhood maltreatment: Effects of trauma history on hippocampal volume, general cognition and subclinical psychosis in healthy adults. *Journal of Psychiatric Research*, *47*(9), 1174-1179. https://doi.org/10.1016/j.jpsychires.2013.05.008

Sar, V., Tutkun, H., Yargic, I., & Kundakci, T. (1999). Con. *Ege Psychiatry Periodics*, *4*, 95–108.

Scher, C. D., Stein, M. B., Asmundson, G. J. G., Mccreary, D. R., & Forde, D. R. (2001). The Childhood Trauma Questionnaire in a community sample: Psychometric properties and normative data. *Journal of Traumatic Stress*, *14*(4), 843–857. https://doi.org/10.1023/A:1013058625719

Schlier, B., Jaya, E. S., Moritz, S., & Lincoln, T. M. (2015). The Community Assessment of Psychic Experiences measures nine clusters of psychosis-like experiences: A validation

of the German version of the CAPE. *Schizophrenia Research, 169*(1–3), 274-279. https://doi.org/10.1016/j.schres.2015.10.034

Scottish Government. (2018, September 04). *Delivering for today, investing for tomorrow: the Government's programme for Scotland 2018-2019*. Scottish Government. https://www.gov.scot/publications/delivering-today-investing-tomorrow-governments-programme-scotland-2018-19

Shah, S., Mackinnon, A., Galletly, C., Carr, V., McGrath, J. J., Stain, H. J., Castle, D., Harvey, C., Sweeney, S., & Morgan, V. A. (2014). Prevalence and impact of childhood abuse in people with a psychotic illness. Data from the second Australian national survey of psychosis. *Schizophrenia Research*, *159*(1), 20-26. https://doi.org/10.1016/j.schres.2014.07.011

Sheffield, J. M., Williams, L. E., Blackford, J. U., & Heckers, S. (2013). Childhood sexual abuse increases risk of auditory hallucinations in psychotic disorders. *Comprehensive Psychiatry*, *54*(7), 1098-1104. https://doi.org/10.1016/j.comppsych.2013.05.013

Shevlin, M., Dorahy, M., & Adamson, G. (2007). Childhood traumas and hallucinations: An analysis of the National Comorbidity Survey. *Journal of Psychiatric Research*, *41*(3–4), 222–228. https://doi.org/10.1016/J.JPSYCHIRES.2006.03.004

Shevlin, M., Murphy, J., Read, J., Mallett, J., Adamson, G., & Houston, J. E. (2011). Childhood adversity and hallucinations: A community-based study using the national comorbidity Survey replication. *Social Psychiatry and Psychiatric Epidemiology*, *46*(12), 1203-1210. https://doi.org/10.1007/s00127-010-0296-x

Siddaway, A. P., Wood, A. M., & Hedges, L. V. (2019). How to Do a Systematic Review: A Best Practice Guide for Conducting and Reporting Narrative Reviews, Meta-Analyses, and Meta-Syntheses. *Annual review of psychology 70*, 747–770. https://doi.org/10.1146/ANNUREV-PSYCH-010418-102803

Sieving, R. E., Beuhring, T., Resnick, M. D., Bearinger, L. H., Shew, M., Ireland, M., & Blum, R. W. (2001). Development of adolescent self-report measures from the National Longitudinal Study of Adolescent Health. *Journal of Adolescent Health*, *28*(1), 73-81. https://doi.org/10.1016/S1054-139X(00)00155-5

Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2011). False-positive psychology: Undisclosed flexibility in data collection and analysis allows presenting anything as significant. *Psychological Science*, *22*(11), 1359-1366. https://doi.org/10.1177/0956797611417632

Smailes, D., Alderson-Day, B., Fernyhough, C., McCarthy-Jones, S., & Dodgson, G. (2015). Tailoring Cognitive Behavioral Therapy to Subtypes of Voice-Hearing. *Frontiers in Psychology*, *6*, 1933. https://doi.org/10.3389/FPSYG.2015.01933

So, S. H. W., Begemann, M. J. H., Gong, X., & Sommer, I. E. (2016). Relationship between neuroticism, childhood trauma and cognitive-affective responses to auditory verbal hallucinations. *Scientific Reports*, *6*(1), 1-8. https://doi.org/10.1038/srep34401

Sommer, I. E., Daalman, K., Rietkerk, T., Diederen, K. M., Bakker, S., Wijkstra, J., & Boks, M. P. M. (2010). Healthy individuals with auditory verbal hallucinations; Who are they? psychiatric assessments of a selected sample of 103 subjects. *Schizophrenia Bulletin*, *36*(3), 633-641. https://doi.org/10.1093/schbul/sbn130

Spalletta, G., Janiri, D., Piras, F., & Sani, G. (2020). *Childhood Trauma in Mental Disorders: A Comprehensive Approach*. Springer International Publishing.

Spitzer, R. L., Williams, J. B. W., Gibbon, M., & First, M. B. (1992). The Structured Clinical Interview for DSM-III-R (SCID): I: History, Rationale, and Description. *Archives of General Psychiatry*, *49*(8), 624-629. https://doi.org/10.1001/archpsyc.1992.01820080032005

Sporle, T., Winter, D., & Rhodes, J. (2011). Childhood sexual abuse and construction of self

and others in people who have experienced psychosis. *Journal of Constructivist Psychology*, *24*(3) 185-207. https://doi.org/10.1080/10720537.2011.571558

Spreen, O. & Benton, A. (2018). *Neurosensory Center Comprehensive Examination for Aphasia: Manual of instructions (NCCEA).* Neuropsychology Laboratory, University of Victoria.

Stamm, B. (1996). *Measurement of stress, trauma, and adaptation.* The Sidran Press.

Steel, C. (2015). Hallucinations as a trauma-based memory: implications for psychological interventions. *Frontiers in Psychology*, *6*, 1262. https://doi.org/10.3389/FPSYG.2015.01262

Steel, C., Fowler, D., & Holmes, E. A. (2005). Trauma-Related Intrusions and Psychosis: An Information Processing Account. *Behavioural and Cognitive Psychotherapy*, *33*(2), 139–152. https://doi.org/10.1017/S1352465804001924

Sugiura, M., Friston, K. J., Willmes, K., Shah, N. J., Zilles, K., & Fink, G. R. (2007). Analysis of intersubject variability in activation: an application to the incidental episodic retrieval during recognition test. *Human brain mapping*, *28*(1), 49-58.

Strauss, J. S. (1969). Hallucinations and Delusions as Points on Continua Function: Rating Scale Evidence. *Archives of General Psychiatry*, *21*(5), 581–586. https://doi.org/10.1001/ARCHPSYC.1969.01740230069010

Sweeney, A., Filson, B., Kennedy, A., Collinson, L., & Gillard, S. (2018). A paradigm shift: relationships in trauma-informed mental health services. *BJPsych Advances*, *24*(5), 319–333. https://doi.org/10.1192/BJA.2018.29

Szucs, D., & Ioannidis, J. P. (2020). Sample size evolution in neuroimaging research: An evaluation of highly-cited studies (1990–2012) and of latest practices (2017–2018) in high-impact journals. *NeuroImage*, *221*, 117164. https://doi.org/10.1016/j.neuroimage.2020.117164

Teicher, M. H., & Samson, J. A. (2016). Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. *Journal of Child Psychology and Psychiatry, 57*(3), 241–266. https://doi.org/10.1111/JCPP.12507

Teicher, M. H., Samson, J. A., Anderson, C. M., & Ohashi, K. (2016). The effects of childhood maltreatment on brain structure, function and connectivity. *Nature Reviews Neuroscience, 17*(10), 652–666. https://doi.org/10.1038/nrn.2016.111

Tell, D., Mathews, H. L., Burr, R. L., & Witek Janusek, L. (2018). During stress, heart rate variability moderates the impact of childhood adversity in women with breast cancer. *Stress*, *21*(2), 179–187. https://doi.org/10.1080/10253890.2018.1424132

Tie, Y., Suarez, R. O., Whalen, S., Radmanesh, A., Norton, I. H., & Golby, A. J. (2009). Comparison of blocked and event-related fMRI designs for pre-surgical language mapping. *NeuroImage*, *47*, T107-T115. https://doi.org/10.1016/J.NEUROIMAGE.2008.11.020

Toh, W. L., Thomas, N., & Rossell, S. L. (2015). Auditory verbal hallucinations in bipolar disorder (BD) and major depressive disorder (MDD): A systematic review. *Journal of Affective Disorders*, *184*, 18–28. https://doi.org/10.1016/J.JAD.2015.05.040

Trauelsen, A. M., Bendall, S., Jansen, J. E., Nielsen, H. G. L., Pedersen, M. B., Trier, C. H., Haahr, U. H., & Simonsen, E. (2015). Childhood adversity specificity and dose-response effect in non-affective first-episode psychosis. *Schizophrenia Research*, *165*(1), 52–59. https://doi.org/10.1016/J.SCHRES.2015.03.014

Üçok, A., & Bikmaz, S. (2007). The effects of childhood trauma in patients with first-episode schizophrenia. *Acta Psychiatrica Scandinavica, 116*(5) 371-377. https://doi.org/10.1111/j.1600-0447.2007.01079.x

United Kingdom Trauma Council. (2020, September). *Beyond the pandemic: Strategic priorities for responding to childhood trauma.* UKTC.

https://uktraumacouncil.link/documents/Coronavirus-CYP-and-Trauma-UKTC-Policy-Briefing-Sept-2020.pdf

Vallejos, M., Cesoni, O. M., Farinola, R., Bertone, M. S., & Prokopez, C. R. (2017). Adverse Childhood Experiences among Men with Schizophrenia. *Psychiatric Quarterly*, *88*(4) 665-673. https://doi.org/10.1007/s11126-016-9487-2

van Harmelen, A. L., van Tol, M. J., Demenescu, L. R., van der Wee, N. J. A., Veltman, D. J., Aleman, A., van Buchem, M. A., Spinhoven, P., Penninx, B. W. J. H., & Elzinga, B. M. (2013). Enhanced amygdala reactivity to emotional faces in adults reporting childhood emotional maltreatment. *Social Cognitive and Affective Neuroscience*, *8*(4) 362-369. https://doi.org/10.1093/scan/nss007

Van Nierop, M., Viechtbauer, W., Gunther, N., Van Zelst, C., De Graaf, R., Ten Have, M., Van Dorsselaer, S., Bak, M., Van Winkel, R., Bruggeman, R., Wiersma, D., Cahn, W., Kahn, R. S., De Haan, L., Meijer, C. J., Myin-Germeys, I., & Van Os, J. (2015). Childhood trauma is associated with a specific admixture of affective, anxiety, and psychosis symptoms cutting across traditional diagnostic boundaries. *Psychological Medicine*, *45*(6), 1277-1288. https://doi.org/10.1017/S0033291714002372

Van Nierop, M., Lataster, T., Smeets, F., Gunther, N., Van Zelst, C., De Graaf, R., Ten Have, M., Van Dorsselaer, S., Bak, M., Myin-Germeys, I., Viechtbauer, W., Van Os, J., & Van Winkel, R. (2014). Psychopathological mechanisms linking childhood traumatic experiences to risk of psychotic symptoms: Analysis of a large, representative population-based sample. *Schizophrenia Bulletin*, *40*(2), S123-S130. https://doi.org/10.1093/schbul/sbt150

Van Os, J., & Reininghaus, U. (2016). Psychosis as a transdiagnostic and extended phenotype in the general population. *World Psychiatry*, *15*(2), 118–124. https://doi.org/10.1002/WPS.20310

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., Read, J., Van Os, J., & Bentall, R. P. (2012). Childhood Adversities Increase the Risk of Psychosis: A Meta-analysis of Patient-Control, Prospective- and Cross-sectional Cohort Studies. *Schizophrenia Bulletin*, *38*(4), 661–671. https://doi.org/10.1093/SCHBUL/SBS050

Vila-Badia, R., Butjosa, A., Del Cacho, N., Serra-Arumí, C., Esteban-Sanjusto, M., Ochoa, S., & Usall, J. (2021). Types, prevalence and gender differences of childhood trauma in first-episode psychosis. What is the evidence that childhood trauma is related to symptoms and functional outcomes in first episode psychosis? A systematic review. *Schizophrenia Research*, *228*, 159–179. https://doi.org/10.1016/J.SCHRES.2020.11.047

Vilhauer, R. P. (2015). Depictions of auditory verbal hallucinations in news media. *International Journal of Social Psychiatry*, *61*(1) 58-63. https://doi.org/10.1177/0020764014535757

Vilhauer, R. P. (2017). Stigma and need for care in individuals who hear voices. *International Journal of Social Psychiatry*, *63*(1), 5–13. https://doi.org/10.1177/0020764016675888

Wainberg, M., Jacobs, G. R., di Forti, M., & Tripathy, S. J. (2021). Cannabis, schizophrenia genetic risk, and psychotic experiences: a cross-sectional study of 109,308 participants from the UK Biobank. *Translational Psychiatry*, *11*(1), 1-9.

Wechsler, D. (1997). *WAIS-III: Wechsler Adult Intelligence Scale (3rd ed.) Administration and scoring manual.* The Psychological Corporation.

Wells, A., & Cartwright-Hatton, S. (2004). A short form of the metacognitions questionnaire: properties of the MCQ-30. *Behaviour Research and Therapy*, *42*(4), 385–396. https://doi.org/10.1016/S0005-7967(03)00147-5

Widom, C. S., & Morris, S. (1997). Accuracy of adult recollections of childhood

victimization: Part 2. Childhood sexual abuse. *Psychological Assessment*, *9*(1), 34–46. https://doi.org/10.1037/1040-3590.9.1.34

Williams, J., Bucci, S., Berry, K., & Varese, F. (2018). Psychological mediators of the association between childhood adversities and psychosis: A systematic review. *Clinical Psychology Review*, *65*, 175–196. https://doi.org/10.1016/J.CPR.2018.05.009

Wing, J. K., Wing, J. K., Babor, T., Brugha, T., Burke, J., Cooper, J. E., Cooper, J. E., Giel, R., Jablenski, A., Regier, D., & Sartorius, N. (1990). SCAN. Schedules for Clinical Assessment in Neuropsychiatry. *Archives of General Psychiatry*, *47*(6) 589-593.

Xie, Y., He, Y., Guan, M., Wang, Z., Zhou, G., Ma, Z., Wang, H., & Yin, H. (2022). Low-frequency rTMS treatment alters the topographical organization of functional brain networks in schizophrenia patients with auditory verbal hallucination. *Psychiatry Research*, *309*, 114393. https://doi.org/10.1016/J.PSYCHRES.2022.114393

Yarkoni, T. (2009). Big correlations in little studies: Inflated fMRI correlations reflect low statistical power—Commentary on Vul et al.(2009). *Perspectives on psychological science*, *4*(3), 294-298.

Young, J. E. . & B. G. (2005). Young Schema Questionnaire-Short Form; Version 3. *APA PsychTests*. https://psycnet.apa.org/doiLanding?doi=10.1037%2Ft67023-000

Yüksel, C., McCarthy, J., Shinn, A., Pfaff, D. L., Baker, J. T., Heckers, S., Renshaw, P., & Öngür, D. (2012). Gray matter volume in schizophrenia and bipolar disorder with psychotic features. *Schizophrenia Research*, *138*(2–3), 177-182. https://doi.org/10.1016/j.schres.2012.03.003

Appendices

Appendix 1 The National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NHLBI, 2014).

Criteria	Yes	No	Other (CD, NR, NA)
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			

Criteria	Yes	No	Other (CD, NR, NA)
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			

Criteria	Yes	No	Other (CD, NR, NA)
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			

Criteria	Yes	No	Other (CD, NR, NA)
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

Appendix 2: Ethical Approval

From: Ethics Application System <ethics@rhul.ac.uk>
Sent: 07 March 2021 09:44
To: Barker, Holly (2019) <Holly.Barker.2019@live.rhul.ac.uk>; Ellett, Lyn <Lyn.Ellett@rhul.ac.uk>; Ethics <Ethics@rhul.ac.uk>
Subject: Result of your application to the Research Ethics Committee (application ID 2508)

PI: Dr Lyn Ellett
Project title: Childhood trauma and frontotemporal activation in the adult brain

REC ProjectID: 2508

Your application has been approved by the Research Ethics Committee.
Please report any subsequent changes that affect the ethics of the project to the University Research Ethics Committee ethics@rhul.ac.uk