Title: A systematic review and meta-analysis of the association between emotional stress reactivity and psychosis

Sarah Muddle*[1], Bradley Jones[1], Dr Gemma Taylor[1] and Dr Pamela Jacobsen[1]

[1] University of Bath, Department of Psychology, Bath, BA2 7AY

* Corresponding author information: University of Bath, Department of Psychology, Bath, BA2 7AY United Kingdom (s.l.muddle@bath.ac.uk), Orcid ID:0000-0002-1023-1481

A systematic review and meta-analysis of the association between emotional stress reactivity and psychosis

Abstract

Aim: Emotional stress reactivity may be a mediating factor in the association between trauma and psychosis. This review aimed to i) identify, summarise and critically evaluate the link between emotional stress reactivity and psychotic experiences ii) examine evidence for a 'dose-response' relationship between stress reactivity and psychosis in the wider psychosis phenotype (i.e. sub-clinical symptoms).

Methods: Electronic database searches (PsychINFO, MEDLINE, EMBASE) were conducted for studies which investigated the link between stress reactivity and psychosis, psychotic symptoms, or a vulnerability to developing psychosis (wider phenotype). Cross-sectional, experimental and experience sampling method study designs were eligible for inclusion.

Results: 45 eligible articles were identified (N participants= 8830). Narrative synthesis showed that increased emotional stress reactivity was associated with psychosis and subclinical psychotic experiences across all study designs, however, findings were inconsistent across studies. The preliminary meta-analysis (k=4, n=383) showed increases in emotional stress reactivity was associated with higher negative affect in response to event-related stress, in those with psychosis compared to controls (mean difference in beta coefficients = 0.05, 95% CI 0.02 to 0.08, p=0.004). However, this difference was small with a considerable degree of heterogeneity (p=.001, I^2 = 81%) so results should be interpreted with caution.

Conclusions: Overall, the evidence suggests that there is a link between emotional stress reactivity and psychosis in those with psychosis, those at high risk of developing psychosis and in relation to subclinical psychotic-like experiences in the general population.

Keywords: Psychotic Disorders; Stress, Psychological; Affect

Introduction

Trauma and Psychosis

The experience of childhood trauma has been shown to be strongly associated with an increased risk of a person later developing psychosis (Read, van Os, Morrison, & Ross, 2005; Varese et al., 2012), including recent evidence for a causal link based on longitudinal data from a large UK cohort study (Croft et al., 2019). It is not yet clear why trauma increases the risk of psychosis, as not all individuals who experience trauma will go on to experience psychosis. This suggests that there may be mediating factors which may partially, or fully, explain the relationship between trauma and the development of psychosis. Understanding more about the mechanisms through which trauma can lead to psychosis can help identify potentially modifiable mediators. Until childhood trauma itself can be fully prevented, the most effective place to intervene is after the trauma and before the development of psychosis.

Emotional Reactivity to Stress

Emotional stress reactivity is a potential modifiable mediator linking trauma and psychosis which could be a target for prevention strategies. Emotional stress reactivity is defined as mood reactivity to daily events and minor disturbances in daily life (Myin-Germeys & van Os, 2007). van Nierop et al. (2018) suggest that some of those exposed to childhood trauma will go on to develop increased stress reactivity, while others will not. This increased level of emotional stress reactivity is associated with higher rates of depressive, anxiety and psychosis symptoms (Lardinois, Lataster, Mengelers, Van Os, & Myin-Germeys, 2011; van Nierop et al., 2018). Several factors may determine the degree to which trauma leads to increased emotional stress reactivity: the severity and number of trauma events (Wichers et al., 2008), later stressful life events (Myin-Germeys, Krabbendam, Delespaul, & Van Os, 2003), genetic factors (Collip, van Winkel, et al., 2011), impact of trauma on the biological stress response (Heim et al., 2000) and psychological and social factors (van Nierop et al., 2018).

Emotional stress reactivity is a proposed mechanism through which daily life events and the subsequent emotional reaction may result in psychotic experiences. Mood reactivity to daily life events is a normal process; however, high levels of mood reactivity in response to daily stressors is problematic and has been linked with a number of mental health difficulties (Myin-Germeys, Peeters, et al., 2003; van Nierop et al., 2018). Experience sampling method has been the main method used to measure emotional stress reactivity through assessing subjective affect and stress in relation to activities and events.

Emotional stress reactivity has been investigated in those at varying points along the continuum of psychotic experiences, in those at high risk of developing psychosis, relatives of those with psychosis and in relation to subclinical psychotic-like experiences (refs). The findings from the first experience sampling method study by Myin-Germeys, Van Os, Schwartz, Stone, and Delespaul (2001) suggested that levels of emotional stress reactivity were highest in those with psychosis, then relatives followed by controls. The authors summarised that the level of vulnerability to psychosis mirrored the level of emotional stress reactivity, in relation to negative affect. Furthermore, in the general population, increased level of subclinical psychotic-like experiences was associated with higher levels of emotional stress reactivity (Lataster et al., 2009). Therefore, the theory that level of vulnerability may be associated with level of emotional stress reactivity may be applied to the continuum of psychotic experiences. Given that there may be evidence of elevated levels of emotional stress reactivity in relatives, this may link with literature on expressed emotion in families leading to development of psychosis (Haidl et al., 2018; Izon, Berry, Law, & French, 2018).

As emotional stress reactivity is a possible modifiable mediator, it could help inform interventions to reduce the risk of psychosis in people exposed to childhood trauma. For example, mindfulness-based interventions have been shown to reduce emotional stress reactivity in individuals with partially-remitted depression (Britton, Shahar, Szepsenwol, & Jacobs, 2012). Interventions such as mindfulness may therefore be used as a preventative measure to reduce psychosis risk in people exposed to childhood trauma.

Three previous literature reviews summarised research on emotional stress reactivity and psychosis and identified that emotional stress reactivity was a plausible mediator between stressful events and psychosis (Holtzman et al., 2013; Myin-Germeys & van Os, 2007; van Winkel, Stefanis, & Myin-Germeys, 2008). However, these were not systematic reviews, so relevant studies could have been missed. In addition, a meta-analysis of 12 studies looked at findings from experience sampling method studies, but focused on positive and negative affect as outcomes, rather than emotional stress reactivity (Cho et al., 2017). Therefore, a systematic literature review has not been conducted on this topic before.

The present review aims to investigate the link between psychosis and emotional stress reactivity using systematic review methods, and quantitative synthesis (preliminary meta-analysis). Given there is research linking the level of psychosis vulnerability with the level of emotional stress reactivity, this review will also investigate the novel questions of whether there is evidence for a dose-response relationship between emotional stress

reactivity and psychosis risk by including studies on the wider psychosis phenotype (e.g. individuals considered at high risk of developing psychosis). This is important as could show the pattern between emotional stress reactivity and vulnerability to psychosis and in turn, could be a target for interventions aimed at preventing the development of distressing psychotic experience as well as for those with psychosis.

The review questions are:
1) Identify, summarise and critically evaluate the link between emotional stress reactivity and psychotic experiences in the general population, those with psychosis and the extended psychosis phenotype.
2) Identify whether there is a 'dose-response' relationship between emotional stress reactivity and psychosis when looking at stress reactivity in those with psychosis, extended psychosis phenotype and non-clinical populations.

Method

Protocol and Registration

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were followed for reporting this review (Page et al., 2021). The protocol for the review, including the inclusion criteria and planned analysis, was registered on PROSPERO prior to the database searches on 6th Dec 2019 and on the Open Science Framework (PROSPERO registration number: CRD42019161304; https://osf.io/cnqhd/). Differences from protocol: the inclusion criterion identifying relevant comparisons was added at stage 2 screening due to discussion between reviewers about uncertainty of inclusion of studies and the updated version of the quality assessment tool was used.

Inclusion and Exclusion Criteria

Study design: Experience sampling method, cross-sectional and experimental approaches were included. In this context, experience sampling method is structured diary technique where participants are instructed to make in the moment ratings of mood and current context several times a day over several days.
Population: Studies were included if participants included were either individuals with a diagnosis of a psychotic disorder, extended psychosis phenotype (i.e., shared familial, demographic, etiological and psychopathological factors with psychotic disorders) or psychotic-like experiences. Studies which included participants with a mixed phenotype where it was not possible to separate out psychosis symptoms were excluded. This may be where participants are experiencing elevated levels of psychotic experiences, anxiety,

and depression and individual levels of psychotic experiences are not reported, as in van Nierop et al. (2018).

Comparison: Studies were included if there was a comparison between groups experiencing different levels of psychosis symptoms or a comparison was made between the level of psychosis symptoms and emotional stress reactivity.

Outcome Measure: Studies were included if there was a self-report measure of emotional stress reactivity, which is defined as mood reactivity to daily events and minor disturbances in daily life (Myin-Germeys, Peeters, et al., 2003). Articles solely including measures of biological stress reactivity were excluded as previous systematic reviews have investigated this topic and changes in emotional stress reactivity can occur in the absence of changes in biological stress reactivity.

Search Strategy

A systematic search of PsychINFO, EMBASE and MEDLINE was conducted using the following search strings: (psychosis OR psychotic OR schizophreni*) AND (stress reactivity OR stress sensitivity OR sensitiv* NEAR/3 stress OR react* NEAR/3 stress). The search strategy was developed by identifying synonyms for psychosis and emotional stress reactivity. Relevant literature was reviewed to assess the different ways the topics were referred by. Furthermore, the index terms related to psychosis were included; the index term most closely related to emotional stress reactivity (stress) was too broad so was not included. Relevant descriptors were sources through MeSH terms. Hallucinations, voices and delusions were assessed as potential search terms but they did not yield any results which did not also include a term such as psychosis or schizophrenia in title, abstract or keywords. See Appendix A for full search terms. The search terms generated were applied to title, abstract and keywords. Reference lists of eligible studies were examined for further eligible studies and lead researchers in this area were contacted to ensure relevant studies were not missed by the search strategy. The search was first conducted on 7th December 2019 and repeated on 22nd January 2021 (33 additional records were found, one of which was eligible and was subsequently included in the review).

Study Selection

Duplicates of records were removed after all the database searches were completed. At stage 1 of screening, the 1st author (S.M.) screened title and abstracts for inclusion. At stage 2, all full-text records were independently double-screened by two reviewers (S.M. and B.J.). Disagreements were initially resolved between the two reviewers and where a unanimous decision was not reached, consensus was reached by consulting the senior author (P.J.).

Data Extraction and Management

(Add something about outcomes extracted for item 10a). Extracted data included: type of publication (e.g. peer reviewed journal), information on the type of participants, participant demographic information (age, gender and ethnicity), number of participants, study design, inclusion/exclusion criteria, country of recruitment, outcome measures and data analyses. The inclusion and exclusion criteria for each group of participants was recorded. The measures used to assess emotional stress reactivity and measures used to assess psychotic symptoms or subclinical psychotic-like experiences were extracted. For experience sampling method studies, specific information on how data was collected was extracted. Corresponding authors were contacted when outcome of interest was not reported in the paper; it was not possible to access data from several studies (see Appendix B). The lead author (S.M.) extracted data for all the studies included. Data was managed using Covidence software (https://www.covidence.org/) during the screening stages of the review and extracted data was inputted into an Excel spreadsheet using a standard template.

Quality Assessment

The Mixed Methods Assessment Tool (M-MAT) was used to assess quality of the studies (Pluye, Gagnon, Griffiths, & Johnson-Lafleur, 2009). The M-MAT is a single integrated tool designed to assess qualitative, quantitative and mixed methods studies. Two screening questions are first applied, i) are there clear research questions and ii) do the data collected address the question(s). The M-MAT is not appropriate when the study does not pass both screening questions. Depending on the study design, one of five categories was used to assess each study, each comprising five assessment criteria. A summary score was calculated by working out the percentage of assessment criteria which were definitely met (e.g. scored as 'yes'). Quality scores therefore ranged from 0, 20, 40, 60, 80 to 100%. 10% of the included studies were double rated by the senior author (P.J.).

Analysis

All eligible studies were incorporated into the narrative descriptive synthesis, which was included due to the heterogeneity of the study designs included. The studies were grouped based on study design to allow for more appropriate comparisons and findings were synthesised highlighting any similarities and differences in study findings and exploring the patterns in the data. Differences in outcome between psychosis, extended psychosis phenotype and controls were assessed, where possible.

A meta-analysis was planned for studies with comparable outcome measures. Experience sampling method studies were most likely to have comparable outcome measure across studies. The most common experience sampling method outcome measure was negative affect event-related stress, so this was planned for use in the meta-analysis. We planned to examine funnel plots for evidence of asymmetry (i.e., small study bias (Deeks, 2020)). Statistical heterogeneity of studies was assessed using I^2. The meta-analysis was conducted in Revman.

Results

Study Selection

Figure 1 (PRISMA diagram) shows the process of how studies were selected. 889 papers were identified through electronic database searches and 28 papers were identified from other sources. After duplicates were removed, titles and abstracts of 679 articles were screened resulting in 93 articles which were included in full-text screen. From full-text screen, 46 eligible articles were identified for inclusion in the review. Eight articles contained overlapping datasets from the same participant samples, and so these were linked together, in order to avoid 'double-counting' of participants across multiple papers reporting analyses from the same dataset. Papers from the same study are grouped together in Table 1, where the papers were part of the same study and the outcome of interest was only reported in one paper, only those findings were reported. When studies have overlapping samples, this is made clear in Table 1 and the separate findings are reported.

[insert Figure 1]

Overview of study design and characteristics

Studies were from the Netherlands (n = 11), Netherlands and Belgium (n = 2), Belgium (n = 3), Netherlands, Belgium and Germany (n=1), Switzerland (n = 2), USA (n = 9), UK (n = 4), Germany (n = 3), New Zealand (n = 2), and Spain (n = 1). 31/37 studies included adult participants, 4/37 studies included participants ranging from adolescents to young adults and 2/37 included only adolescents. 13/38 studies included general population samples, 6/38 included individuals with psychosis (four with healthy control comparison), 5/38 included individuals with extended psychosis phenotype compared with controls, 11/38 included both psychosis and extended psychosis phenotype (ten with healthy controls comparison), 1/38 included mental health service users, siblings and controls and 1/38 included those with schizotypal personality disorder. Experience sampling method design was used in 20/38 studies, cross-sectional design in 11/38 and experimental in 6/38 studies. See Table 1 for summary, the table has been structured by study design and the participant details, measurement of psychosis or psychotic-like experiences, outcome of interest and the main relevant findings and direction of the effect are reported for each study along with the M-MAT study design and the percentage summary for the quality assessment. The M-MAT quality assessment information is summarised in Table 2 and Table 3 based on the study design.

[Insert Table 1]

[Insert Table 2]

[Insert Table 3]

Narrative Synthesis

1. Experience Sampling Method

20/38 of the studies which met the criteria for the review used experience sampling method. Experience sampling method is considered to be a gold standard approach as assessments are completed in the moment during normal daily life, so the approach is both ecologically valid and not susceptible to recall bias. However, it is time consuming and demanding for participants. In terms of the stress measures, most studies included event-related, activity-related and/or social stress. Affect was typically measured in terms of negative affect, some studies additionally included positive affect. All outcomes were measured on similar or the same Likert scales.

1.1. General Population

Six studies used general population samples and looked at the association between emotional stress reactivity and subclinical psychotic-like experiences. Four of the studies found increased emotional stress reactivity was associated with greater subclinical psychotic symptoms or positive schizotypy (Chun, Barrantes-Vidal, Sheinbaum, & Kwapil, 2017; Collip, Wigman, et al., 2013; Kramer et al., 2014; Lataster et al., 2009). Two studies did not find a significant association between emotional stress reactivity and subclinical psychosis symptoms or momentary paranoia (Booij, Snippe, Jeronimus, Wichers, & Wigman, 2018; Vaessen et al., 2017). In the study by Vaessen et al. (2017), there was a difference in age, gender and levels of emotional stress reactivity between completers and non-completers of the study, therefore, there appears to be a non-response bias. Four of the above studies recruited participants from the East Flanders Twin Survey in Belgium, however, it is unclear if there is an overlap in participants across the studies (Collip, Habets, et al., 2013; Kramer et al., 2014; Lataster et al., 2009; Vaessen et al., 2017).

1.2. Individuals with Psychosis

Three studies investigated the relationship between stress reactivity and psychotic symptoms in individuals with psychosis. Both Lataster, Valmaggia, Lardinois, van Os, and Myin-Germeys (2013) (n = 64) and Reininghaus, Kempton, et al. (2016) (n = 51) found positive psychotic symptoms were associated with greater negative affect in response to stressful situations. However, Westermann et al. (2017) did not find an association between positive psychotic symptoms and stress sensitivity. In this study, the measure of stress sensitivity consisted of assessment of momentary emotional state in respect of valence and arousal, which differs from emotional stress reactivity. Furthermore, the null finding may be due to low power from including only 15 participants.

Seven studies compared those with psychosis with controls and five found increased emotional stress reactivity in those with psychosis compared to controls (Frissen et al., 2014; Habets et al., 2012; Myin-Germeys et al., 2001; Reininghaus, Kempton, et al., 2016; van Winkel et al., 2008). Higher emotional stress reactivity was not always found for all measurements of stress. For example, van der Steen et al. (2017) and Reininghaus, Kempton, et al. (2016) found the effect of higher negative affect in response to activity-related stress, but not event-related or social stress. One of the above studies investigated the link between activity-related stress effecting psychotic symptoms via negative affect and found a non-significant trend towards this being greater in individuals with psychosis compared to controls (p=.072) (Klippel et al., 2017). Another study found no significant differences in emotional responses to stress in individuals with psychosis compared to controls (Palmier-Claus, Dunn, & Lewis, 2012). However, Palmier-Claus et al. (2012) had a high drop out of individuals with psychosis (n =27) which may have led to a biased sample.

1.3. Extended phenotype (relatives/UHR)

Five studies compared individuals with psychosis to relatives and all studies demonstrated higher emotional stress reactivity in those with psychosis compared to relatives (Frissen et al., 2014; Habets et al., 2012; Lataster, Collip, Lardinois, Van Os, & Myin-Germeys, 2010; Myin-Germeys et al., 2001; Pos et al., 2017). Three studies compared emotional stress reactivity between relatives and controls and all studies found no significant difference (Collip, Nicolson, et al., 2011; Frissen et al., 2014; Habets et al., 2012). The only quality issues identified were high rates of excluded participants and a lack of gender covariate in Pos et al. (2017) and Myin-Germeys et al. (2001). Rauschenberg et al. (2017) compared emotional stress reactivity in mental health service users, with higher levels of psychotic symptoms, with siblings of service users. This study demonstrated greater stress reactivity in service users compared to siblings. However, service users scored higher on measures of anxiety and depression as well as on measures of psychotic symptoms.

Three studies, comparing those at risk of developing psychosis with controls, found emotional stress reactivity was higher in those at high risk (Palmier-Claus et al., 2012; Reininghaus, Kempton, et al., 2016; van der Steen et al., 2017). Four studies compared individuals with psychosis to those at high risk of developing psychosis. In three of the studies, emotional stress reactivity was higher in those at high risk compared with individuals with psychosis (Palmier-Claus et al., 2012; Reininghaus, Kempton, et al., 2016; van der Steen et al., 2017). Vaessen et al. (2019) combined data from several studies and compared those with chronic psychosis with those in early stages of psychosis, either first-episode or clinical high risk. This study found greater initial negative

affect in response to event-related stress and slower affective recovery to stressors in early psychosis compared to chronic psychosis and healthy controls.

2. Experimental Design

Six of the studies used an experimental paradigm to assess emotional responses to a stressor, two articles were from the same study (Lincoln, Hartmann, Köther, & Moritz, 2015; Lincoln, Köther, Hartmann, Kempkensteffen, & Moritz, 2015) and one paper was missing data which was included in another study (Veling, Counotte, Pot-Kolder, Van Os, & Van Der Gaag, 2016; Veling, Pot-Kolder, Counotte, van Os, & van der Gaag, 2016). In this study design, ratings of affect are completed following an experimental stressor, so the results are less vulnerable to recall bias. However, the approach has limited ecological validity as it is conducted in a laboratory setting.

2.1. Individuals with psychosis and high risk of psychosis

Four of these studies compared individuals with psychosis, one study also included individuals at ultra-high risk of psychosis, with controls (Dinzeo, Cohen, Nienow, & Docherty, 2008; Horan & Blanchard, 2003; Jongeneel, Pot-Kolder, Counotte, van der Gaag, & Veling, 2018; Lincoln, Köther, et al., 2015). Two of those studies found individuals with psychosis, or those with higher vulnerability for psychosis, experienced greater negative affect in response to a stressor than controls (Jongeneel et al., 2018; Lincoln, Köther, et al., 2015), while two did not (Dinzeo et al., 2008; Horan & Blanchard, 2003). This difference in findings could be due to methodological differences in how stress reactivity was measured. Similarly, Veling, Pot-Kolder, et al. (2016) compared those with high psychosis (psychosis and high risk) liability to those with low liability (relatives and controls) and found greater subjective distress in response to stressors in high liability. Another study compared those at risk of psychosis with controls and first-degree relatives and found higher negative affect in response to a social stressor in the high risk group compared with controls (Söder, Krkovic, & Lincoln, 2020).

2.2. Relatives of individuals with psychosis

Two studies compared relatives with controls and did not find a significant difference in subjective stress or negative affect in response to a stressor (Lincoln, Köther, et al., 2015; Söder et al., 2020).

3. Cross-Sectional Design

12 studies used a cross-sectional design to assess emotional stress reactivity and psychosis vulnerability or psychotic-like experiences using questionnaires. This approach can yield large data sets and the sample size of these studies range from 79 to 945. However, self-report questionnaires rely on accurate retrospective memory of participants, therefore, reports may be vulnerable to recall bias.

3.1. General Population

Seven of the studies investigated the link between subclinical psychotic experiences and stress reactivity in the general population. All seven studies demonstrated a positive association between levels of stress sensitivity and psychotic-like experiences, effect sizes range from medium to high (DeVylder & Hilimire, 2015; Gibson et al., 2014; Gibson, Reeves, Cooper, Olino, & Ellman, 2019; Grattan & Linscott, 2019; Laloyaux, Dessart, Van Der Linden, Lemaire, & Larøi, 2016; Rössler, Ajdacic-Gross, Rodgers, Haker, & Müller, 2016; Ruzibiza, Grattan, Eder, & Linscott, 2018). This suggests that higher levels of subclinical psychotic-like experiences are associated with greater stress sensitivity.

3.2. Individuals at high risk of developing psychosis

All four studies, investigating the link between stress reactivity and those at high risk of developing psychosis compared to controls, found evidence for greater stress sensitivity for adults and children at high risk of developing psychosis, with medium to high effect sizes (Cullen, Fisher, Roberts, Pariante, & Laurens, 2014; DeVylder et al., 2013; Moskow et al., 2016; Trotman et al., 2014). In the study by Cullen et al. (2014), children with multiple antecedents of schizophrenia (n=29) experienced greater distress to daily stressors, compared to typically developing children (n=42), and in more domains than children with family history of schizophrenia (n=19). Different questionnaires were used in each of these studies, and these measures may not fully encompass emotional stress reactivity. Furthermore, the measure used by Cullen et al. (2014) does not appear to have been assessed for psychometric properties. Two studies investigated distress in relation to daily stressors, which appears to more accurately represent emotional stress reactivity, and found higher rates of distress in those with schizotypal personality disorder in comparison to other personality disorders and controls, and those at high risk of developing psychosis compared to controls (Tessner, Mittal, & Walker, 2011).

Preliminary Meta-Analysis

Individuals with psychosis vs. healthy controls

For negative affect in response to event-related stress, four experience sampling method studies (n= 383) provided data for the meta-analysis. Of the 20 experience sampling

method studies, only 10 made comparisons between individuals with psychosis, those at high-risk, relatives and/or controls. The frequency of different experience sampling method outcome measures was calculated, and the most used outcome measure was selected for the meta-analysis (negative affect event-related stress) with the most commonly used comparison (individuals with psychosis vs controls). Figure 2 illustrates the decision tree for including studies, only 4 studies reported the outcome of interest and the necessary analysis to be included. Insufficient data was available for other comparisons to be included in the meta-analysis. Due to the small sample size, this meta-analysis only summarises preliminary findings and requires more data to be able to generalise findings. (Report where had to transform data to prepare for meta-analysis (item 13b))

Each study included in the meta-analysis consisted of two linear regression models (one for psychosis group, one for control group) which represent the association between event-related stress and mood between the psychosis and control groups. The effect estimates extracted from papers was the beta co-efficients from the multilevel linear regression models for psychosis group and the control group within each study. Due to the variability in participant characteristics and study characteristics, a random-effects model was selected.

Four studies compared those with psychosis with controls on negative affect event-related stress. Two of the studies were assessed to be high quality using the M-MAT (Frissen et al., 2014; Reininghaus, Kempton, et al., 2016); one study did not include relevant confounding variables (Myin-Germeys et al., 2001) and one study had quality issues (van Winkel et al., 2008). Emotional stress reactivity is measured by self-report assessment of current event-related stress (how unpleasant is the most recent event) and current negative affect, at multiple time points. All studies except for van Winkel et al. (2008) where participants completed ratings 12 times a day, participants completed self-assessment ratings 10 times a day for six consecutive days. Event-related stress was measured consistently across all studies; three studies measured negative affect with five mood adjectives on a 7-point likert scale (Myin-Germeys et al., 2001; Reininghaus, Kempton, et al., 2016; van Winkel et al., 2008), Frissen et al. (2014) used six mood adjectives. From the data reported, it was not possible to access unadjusted analysis from all studies, therefore, some studies include covariates. These covariates differed somewhat between studies. The model comparing individuals with psychosis with controls reveals a small mean difference in beta co-efficient of 0.05 (95% CI 0.02 - 0.08, p=0.004), see Figure 2. This demonstrates a small and relatively precise best estimate for average effect indicating higher emotional stress reactivity in those with psychosis compared to controls.

[Insert Figure 3]

There were insufficient studies (<10) to use a funnel plot, therefore, there was no formal way to assess for publication bias (Deeks, 2020). I^2 was 81%, indicating considerable statistical heterogeneity (Deeks, 2020), therefore, the results from the meta-analysis should be interpreted with caution as the meta-analysis outcome is not representative for the studies included.

Discussion

This review aimed to 1) identify, summarise and critically evaluate the link between emotional stress reactivity and psychotic experiences and 2) identify whether there is a dose-dependent relationship between psychosis vulnerability and emotional stress reactivity. Three main approaches used to assess emotional stress reactivity include experimental stress paradigms, experience sampling method and cross-sectional questionnaires. Overall, the findings of the current review suggest an inconsistent, positive association between emotional stress reactivity and psychotic experiences in both clinical and non-clinical populations.

In terms of strengths and limitations of the review, the search strategy and research questions were published in advance on the PROSPERO database and Open Science Framework, increasing transparency and reproducibility of the work. This review attempted to include all research relevant to the research questions by including the multiple different ways emotional stress reactivity may be referred to in the literature and by not limiting the publication dates. However, as only studies published in English were included, this may have led to relevant studies being excluded. The review only included peer-reviewed articles, however due to publication bias, negative or null findings may have been under-represented in the literature. Despite efforts to access unpublished data from eligible studies to add to the narrative synthesis and meta-analysis, this was not possible for several studies which limits the synthesis of findings. In the meta-analysis, regression data was used and there is debate in the literature over whether beta co-efficient are appropriate to use in meta-analyses (Peterson & Brown, 2005). However, as the data included in this meta-analysis consisted of a comparison of two regression equations per study, beta co-efficient were considered appropriate to use for mean effect sizes.

The current review found that, for individuals with psychosis, there is some evidence suggesting they tend to have higher levels of emotional stress reactivity or subjective

stress sensitivity compared to healthy controls. However, this finding is not consistent across all studies, with differences in methodology and ways of measuring emotional stress reactivity likely contributing to the heterogeneity in the published literature. Our preliminary meta-analysis of four studies suggests there may be a small effect indicating emotional stress reactivity was higher in those with psychosis; however, there was high variability in findings between different studies. Therefore, the findings should be interpreted with caution as the meta-analysis outcome for the studies included is not representative and there is limited generalisability of the findings due to the small sample size. The high heterogeneity may be in part due to the differences in covariates included in each study which may have effected the strength of the relationship and this makes the findings of the meta-analysis harder to interpret. The inconsistency in findings may be accounted for by genetic (Collip, van Winkel, et al., 2011; van Winkel et al., 2008) and environmental differences, such as previous interventions and medication, across different study samples (Palmier-Claus et al., 2012; van der Steen et al., 2017). Due to the small sample size and high heterogeneity, more data is required to investigate whether the findings of this preliminary meta-analysis are reliable. Moderators were not explored in the meta-analysis, this could be considered in future research.

In terms of the extended psychosis phenotype, for those at high risk of developing psychosis, there was consistent evidence from experience sampling method and cross-sectional studies for higher emotional stress reactivity in the high-risk group compared with controls. In contrast, some experimental and all experience sampling method studies suggested that there was no difference in emotional stress reactivity between relatives of individuals with psychosis and controls. Given the lack of evidence for elevated emotional stress reactivity in relatives, these findings do not support the link between emotional stress reactivity and high expressed emotion and the development of psychosis. Despite the lack of evidence for increased emotional stress reactivity in relatives, there is evidence for increased cortisol reactivity in response to stressors (Collip, Nicolson, et al., 2011). Therefore, although relatives may have a biological stress reactivity vulnerability, they may have a protective mechanism (Collip, Nicolson, et al., 2011); this may reflect greater coping skills or emotional resilience in relatives.

In relation to the second research question, it is unclear whether there is a dose-dependent relationship between psychosis vulnerability and emotional stress reactivity. Although those at high risk of developing psychosis, and some individuals with psychosis, had higher emotional stress reactivity than controls, relatives of those with psychosis tended to not differ from controls. Furthermore, there is some evidence to suggest that

those at high risk have greater emotional stress reactivity than those with psychosis (Palmier-Claus et al., 2012; van der Steen et al., 2017).

In terms of common limitations for the studies included, one of the main quality issues associated with experience sampling method studies was the high dropout rate of participants and high rates of excluded participants due to insufficient experience sampling method responses. This may have biased samples, possibly towards those with lower symptomology or those who faced fewer stressors. Across different study designs, it was not always clear from the articles whether all participants contributed to all of the data, therefore, missing data similarly may have biased the findings. In addition, gender differences in emotional stress reactivity have been previously identified and not all studies included this as a potentially confounding variable. All studies were conducted in Western countries and most participants were white European. 16 of the studies did not report ethnicity which limits the ability to draw conclusions about the generalisability of findings. Therefore, the findings may not be reliable in non-Western cultures and with people from different ethnic backgrounds.

Research and Clinical Implications

Overall, in this review, there is evidence linking increased emotional stress reactivity with psychosis and psychotic-like experiences. When linking to the wider literature, research suggests emotional stress reactivity may be a pathway through which trauma can result in psychosis (van Nierop et al., 2018). In line with this theory, childhood trauma has been linked with a sensitised stress response with increased negative affect to daily stressors and later psychotic experiences (Cristobal-Narvaez et al., 2016). Furthermore, research has demonstrated a pattern of resilience, through lower levels of emotional stress reactivity, in individuals with childhood trauma without mental health difficulties (Rauschenberg et al., 2017).

The findings of this study suggest emotional stress reactivity could be the target of interventions for those at risk of developing psychosis and may result in a positive impact on the development of psychosis, level of distress and/or ability to manage the impact of daily life stressors. The inconsistent relationship between emotional stress reactivity and individuals with psychosis may reflect developed coping skills or received interventions which help to manage their emotional response to stressors.

Mindfulness-based cognitive therapy has been shown to have a positive impact at reducing emotional stress reactivity in individuals with depression (Britton et al., 2012). Therefore, mindfulness-based interventions may be a possible candidate for improving

outcomes for individuals at high risk of developing psychosis through the impact on emotional stress reactivity. Mindfulness-based interventions have an existing strong evidence base demonstrating beneficial effects on symptoms in those with psychosis (Louise, Fitzpatrick, Strauss, Rossell, & Thomas, 2018). Further research is needed to investigate whether these interventions have the same effect on emotional stress reactivity in individuals with psychosis and those at high risk. A recent review suggested that mindfulness-based interventions can be effective at improving levels of distress, anxiety, low mood and quality of life in those with first-episode psychosis (Vignaud, Reilly, Donde, Haesebaert, & Brunelin, 2019). This review highlighted the paucity of research investigating the use of these interventions with those at high risk of developing psychosis; only one study examined the use of these interventions with those at ultra-high risk (Alvarez-Jimenez et al., 2018). Further research is needed to assess whether these interventions are useful for this high-risk group.

Mindfulness-based interventions could be targeted earlier at a population level to reduce the likelihood of individuals needing to access mental health services. For example, the MYRIAD trial is investigating the impact of mindfulness training for adolescence in schools (Kuyken et al., 2017). This form of intervention could help to reduce emotional stress reactivity across the population and prevent the development of mental health difficulties. Alternatively, interventions and preventative approaches could focus on reducing the stressfulness of the environment. This approach has been applied in family intervention studies where reduced stress in the social environment resulted in decreased risk of relapse in those with psychosis (Leff, 1994).

In summary, emotional stress reactivity is associated with the development of subclinical and clinical psychotic experiences (Myin-Germeys & van Os, 2007). The inconsistency across different studies suggests that this pathway may be one of several possible pathways to psychosis. When linking with the wider literature, trauma exposure may lead to increased emotional stress reactivity in some individuals and contribute to the development of mental health difficulties (van Nierop et al., 2018). Early intervention strategies which target emotional stress reactivity may be beneficial in protecting against future risk of developing affective and psychotic symptoms.

Funding/Support: No financial or non-financial support was received for this review.

Conflict of interest statement: There are no conflicts of interest to declare.

Availability of Data: Extracted data for the narrative synthesis, quality assessment and meta-analysis will be stored in the University repository.

References

Alvarez-Jimenez, M., Gleeson, J., Bendall, S., Penn, D., Yung, A., Ryan, R., . . . Miles, C. (2018). Enhancing social functioning in young people at Ultra High Risk (UHR) for psychosis: A pilot study of a novel strengths and mindfulness-based online social therapy. *Schizophrenia Research, 202*, 369-377.

Booij, S. H., Snippe, E., Jeronimus, B. F., Wichers, M., & Wigman, J. T. W. (2018). Affective reactivity to daily life stress: Relationship to positive psychotic and depressive symptoms in a general population sample. *Journal of Affective Disorders, 225*, 474-481. doi:10.1016/j.jad.2017.08.051

Britton, W. B., Shahar, B., Szepsenwol, O., & Jacobs, W. J. (2012). Mindfulness-Based Cognitive Therapy Improves Emotional Reactivity to Social Stress: Results from a Randomized Controlled Trial. *Behavior Therapy, 43*(2), 365-380. doi:10.1016/j.beth.2011.08.006

Cho, H., Gonzalez, R., Lavaysse, L. M., Pence, S., Fulford, D., & Gard, D. E. (2017). Do people with schizophrenia experience more negative emotion and less positive emotion in their daily lives? A meta-analysis of experience sampling studies. *Schizophrenia Research, 183*, 49-55. doi:10.1016/j.schres.2016.11.016

Chun, C. A., Barrantes-Vidal, N., Sheinbaum, T., & Kwapil, T. R. (2017). Expression of schizophrenia-spectrum personality traits in daily life. *Personality disorders, 8*(1), 64-74. doi:10.1037/per0000141

Collip, D., Habets, P., Marcelis, M., Gronenschild, E., Lataster, T., Lardinois, M., . . . Myin-Germeys, I. (2013). Hippocampal volume as marker of daily life stress sensitivity in psychosis. *Psychological Medicine, 43*(7), 1377-1387.

Collip, D., Nicolson, N. A., Lardinois, M., Lataster, T., van Os, J., Myin-Germeys, I., & G.R.O.U.P. (2011). Daily cortisol, stress reactivity and psychotic experiences in individuals at above average genetic risk for psychosis. *Psychological Medicine, 41*(11), 2305-2315.

Collip, D., van Winkel, R., Peerbooms, O., Lataster, T., Thewissen, V., Lardinois, M., . . . Myin-Germeys, I. (2011). COMT Val158Met-stress interaction in psychosis: Role of background psychosis risk. *CNS Neuroscience and Therapeutics, 17*(6), 612-619. doi:10.1111/j.1755-5949.2010.00213.x

Collip, D., Wigman, J. T. W., Myin-Germeys, I., Jacobs, N., Derom, C., Thiery, E., . . . van Os, J. (2013). From Epidemiology to Daily Life: Linking Daily Life Stress Reactivity to Persistence of Psychotic Experiences in a Longitudinal General Population Study. *PLoS ONE, 8*(4). doi:10.1371/journal.pone.0062688

Cristobal-Narvaez, P., Sheinbaum, T., Ballespi, S., Mitjavila, M., Myin-Germeys, I., Kwapil, T. R., & Barrantes-Vidal, N. (2016). Impact of Adverse Childhood Experiences on Psychotic-Like Symptoms and Stress Reactivity in Daily Life in Nonclinical Young Adults. *PLoS ONE, 11*(4), e0153557-e0153557. doi:10.1371/journal.pone.0153557

Croft, J., Heron, J., Teufel, C., Cannon, M., Wolke, D., Thompson, A., . . . Zammit, S. (2019). Association of trauma type, age of exposure, and frequency in childhood and adolescence with psychotic experiences in early adulthood. *JAMA psychiatry, 76*(1), 79-86.

Cullen, A. E., Fisher, H. L., Roberts, R. E., Pariante, C. M., & Laurens, K. R. (2014). Daily stressors and negative life events in children at elevated risk of developing schizophrenia. *British Journal of Psychiatry, 204*(5), 354-360. doi:10.1192/bjp.bp.113.127001

Deeks, J. J., Higgins, J. P. T., Altman, D. G. . (2020). Chapter 10: Analysing data and undertaking meta-analyses. In. J. P. T. Higgins, Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., Welch, V.A (Series Ed.), *Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020).*

DeVylder, J. E., Ben-David, S., Schobel, S. A., Kimhy, D., Malaspina, D., & Corcoran, C. M. (2013). Temporal association of stress sensitivity and symptoms in individuals at clinical high risk for psychosis. *Psychological Medicine, 43*(2), 259-268. doi:10.1017/S0033291712001262

DeVylder, J. E., & Hilimire, M. R. (2015). Suicide Risk, Stress Sensitivity, and Self-Esteem among Young Adults Reporting Auditory Hallucinations. *Health & social work, 40*(3), 175-181.

Dinzeo, T. J., Cohen, A. S., Nienow, T. M., & Docherty, N. M. (2008). Arousability in schizophrenia: Relationship to emotional and physiological reactivity and symptom severity. *Acta Psychiatrica Scandinavica, 117*(6), 432-439. doi:10.1111/j.1600-0447.2008.01185.x

Frissen, A., Lieverse, R., Drukker, M., Delespaul, P., Lataster, T., Myin-Germeys, I., & van Os, J. (2014). Evidence that childhood urban environment is associated with blunted stress reactivity across groups of patients with psychosis, relatives of patients and controls. *Social psychiatry and psychiatric epidemiology, 49*(10), 1579-1587. doi:10.1007/s00127-014-0859-3

Gibson, L. E., Anglin, D. M., Klugman, J. T., Reeves, L. E., Fineberg, A. M., Maxwell, S. D., . . . Ellman, L. M. (2014). Stress sensitivity mediates the relationship between traumatic life events and attenuated positive psychotic symptoms differentially bygender in a college population sample. *Journal of Psychiatric Research, 53*(1), 111-118. doi:10.1016/j.jpsychires.2014.02.020

Gibson, L. E., Reeves, L. E., Cooper, S., Olino, T. M., & Ellman, L. M. (2019). Traumatic life event exposure and psychotic-like experiences: A multiple mediation model of cognitive-based mechanisms. *Schizophrenia Research, 205*, 15-22. doi:10.1016/j.schres.2018.02.005

Glaser, J. P., Os, J. V., Mengelers, R., & Myin-Germeys, I. (2008). A momentary assessment study of the reputed emotional phenotype associated with borderline personality disorder. *Psychological Medicine, 38*(9), 1231-1239. doi:10.1017/S0033291707002322

Grattan, R. E., & Linscott, R. J. (2019). Components of schizophrenia liability affect the growth of psychological stress sensitivity following major life events. *Schizophrenia Research, 212*, 134-139. doi:10.1016/j.schres.2019.07.056

Habets, P., Collip, D., Myin-Germeys, I., Gronenschild, E., van Bronswijk, S., Hofman, P., . . . Marcelis, M. (2012). Pituitary volume, stress reactivity and genetic risk for psychotic disorder. *Psychological Medicine, 42*(7), 1523-1533. doi:10.1017/S0033291711002728

Haidl, T., Rosen, M., Schultze-Lutter, F., Nieman, D., Eggers, S., Heinimaa, M., . . . Linszen, D. (2018). Expressed emotion as a predictor of the first psychotic episode—Results of the European prediction of psychosis study. *Schizophrenia Research, 199*, 346-352.

Heim, C., Newport, D. J., Heit, S., Graham, Y. P., Wilcox, M., Bonsall, R., . . . Nemeroff, C. B. (2000). Pituitary-Adrenal and Autonomic Responses to Stress in Women After Sexual and Physical Abuse in Childhood. *JAMA : the journal of the American Medical Association, 284*(5), 592-597. doi:10.1001/jama.284.5.592

Heubeck, B., & O'Sullivan, C. (1998). An exploration into the nature, frequency and impact of school hassles in the middle school years. *Australian Psychologist, 33*(2), 130-137.

Holtzman, C. W., Trotman, H. D., Goulding, S. M., Ryan, A. T., MacDonald, A. N., Shapiro, D. I., . . . Walker, E. F. (2013). Stress and neurodevelopmental processes in the emergence of psychosis. *Neuroscience, 249*, 172-191. doi:10.1016/j.neuroscience.2012.12.017

Horan, W. P., & Blanchard, J. J. (2003). Emotional responses to psychosocial stress in schizophrenia: The role of individual differences in affective traits and coping. *Schizophrenia Research, 60*(2-3), 271-283. doi:10.1016/S0920-9964(02)00227-X

Izon, E., Berry, K., Law, H., & French, P. (2018). Expressed emotion (EE) in families of individuals at-risk of developing psychosis: A systematic review. *Psychiatry Research, 270*, 661-672.

Jongeneel, A., Pot-Kolder, R., Counotte, J., van der Gaag, M., & Veling, W. (2018). Self-esteem moderates affective and psychotic responses to social stress in psychosis: A virtual reality study. *Schizophrenia Research, 202*, 80-85. doi:10.1016/j.schres.2018.06.042

Klein, C., Andresen, B., & Jahn, T. (1997). Erfassung der schizotypen Persönlichkeit nach DSM-III-R: Psychometrische Eigenschaften einer autorisierten deutschsprachigen Übersetzung des" Schizotypal Personality Questionnaire"(SPQ) von Raine. *Diagnostica, 43*, 347-369.

Klippel, A., Myin-Germeys, I., Chavez-Baldini, U., Preacher, K. J., Kempton, M., Valmaggia, L., . . . Reininghaus, U. (2017). Modeling the Interplay Between Psychological Processes and Adverse, Stressful Contexts and Experiences in Pathways to Psychosis: An Experience Sampling Study. *Schizophrenia Bulletin, 43*(2), 302-315. doi:10.1093/schbul/sbw185

Kramer, I., Simons, C. J. P., Wigman, J. T. W., Collip, D., Jacobs, N., Derom, C., . . . Wichers, M. (2014). Time-lagged moment-to-moment interplay between negative affect and paranoia: New insights in the affective pathway to psychosis. *Schizophrenia Bulletin, 40*(2), 278-286. doi:10.1093/schbul/sbs194

Kuyken, W., Nuthall, E., Byford, S., Crane, C., Dalgleish, T., Ford, T., . . . the, M. t. (2017). The effectiveness and cost-effectiveness of a mindfulness training programme in schools compared with normal school provision (MYRIAD): study protocol for a randomised controlled trial. *Trials, 18*(1), 194. doi:10.1186/s13063-017-1917-4

Laloyaux, J., Dessart, G., Van Der Linden, M., Lemaire, M., & Larøi, F. (2016). Maladaptive emotion regulation strategies and stress sensitivity mediate the relation between adverse life events and attenuated positive psychotic symptoms. *Cognitive Neuropsychiatry, 21*(2), 116-129. doi:10.1080/13546805.2015.1137213

Lardinois, M., Lataster, T., Mengelers, R., Van Os, J., & Myin-Germeys, I. (2011). Childhood trauma and increased stress sensitivity in psychosis. *Acta Psychiatrica Scandinavica, 123*(1), 28-35.

Lataster, T., Collip, D., Lardinois, M., Van Os, J., & Myin-Germeys, I. (2010). Evidence for a familial correlation between increased reactivity to stress and positive psychotic symptoms. *Acta Psychiatrica Scandinavica, 122*(5), 395-404. doi:10.1111/j.1600-0447.2010.01566.x

Lataster, T., Valmaggia, L., Lardinois, M., van Os, J., & Myin-Germeys, I. (2013). Increased stress reactivity: a mechanism specifically associated with the positive symptoms of psychotic disorder. *Psychological Medicine, 43*(7), 1389-1400.

Lataster, T., Wichers, M., Jacobs, N., Mengelers, R., Derom, C., Thiery, E., . . . Myin-Germeys, I. (2009). Does reactivity to stress cosegregate with subclinical psychosis? A general population twin study. *Acta Psychiatrica Scandinavica, 119*(1), 45-53. doi:10.1111/j.1600-0447.2008.01263.x

Leff, J. (1994). Stress reduction in the social-environment of schizophrenic-patients. *Acta Psychiatrica Scandinavica, 90*, 133-139. doi:10.1111/j.1600-0447.1994.tb05902.x

Lincoln, T., Hartmann, M., Köther, U., & Moritz, S. (2015). Dealing with feeling: Specific emotion regulation skills predict responses to stress in psychosis. *Psychiatry Research, 228*(2), 216-222. doi:10.1016/j.psychres.2015.04.003

Lincoln, T., Köther, U., Hartmann, M., Kempkensteffen, J., & Moritz, S. (2015). Responses to stress in patients with psychotic disorders compared to persons with varying levels of vulnerability to psychosis, persons with depression and healthy controls. *Journal of Behavior Therapy and Experimental Psychiatry, 47*, 92-101. doi:10.1016/j.jbtep.2014.11.011

Loewy, R. L., Johnson, J. K., & Cannon, T. D. (2007). Self-report of attenuated psychotic experiences in a college population. *Schizophrenia Research, 93*(1-3), 144-151.

Louise, S., Fitzpatrick, M., Strauss, C., Rossell, S. L., & Thomas, N. (2018). Mindfulness- and acceptance-based interventions for psychosis: Our current understanding and a meta-analysis. *Schizophrenia Research, 192*, 57-63. doi:10.1016/j.schres.2017.05.023

Moskow, D. M., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., Heinssen, R., . . . Seidman, L. J. (2016). The relations of age and pubertal development with cortisol and daily stress in youth at clinical risk for psychosis. *Schizophrenia Research, 172*(1-3), 29-34.

Myin-Germeys, I., Krabbendam, L., Delespaul, P. A. E. G., & Van Os, J. (2003). Do life events have their effect on psychosis by influencing the emotional reactivity to daily life stress? *Psychological Medicine, 33*(2), 327-333. doi:10.1017/S0033291702006785

Myin-Germeys, I., Peeters, F., Havermans, R., Nicolson, N. A., DeVries, M. W., Delespaul, P., & Van Os, J. (2003). Emotional reactivity to daily life stress in psychosis and affective disorder: An experience sampling study. *Acta Psychiatrica Scandinavica, 107*(2), 124-131. doi:10.1034/j.1600-0447.2003.02025.x

Myin-Germeys, I., & van Os, J. (2007). Stress-reactivity in psychosis: Evidence for an affective pathway to psychosis. *Clinical Psychology Review, 27*(4), 409-424. doi:10.1016/j.cpr.2006.09.005

Myin-Germeys, I., Van Os, J., Schwartz, J. E., Stone, A. A., & Delespaul, P. A. (2001). Emotional reactivity to daily life stress in psychosis. *Archives of General Psychiatry, 58*(12), 1137-1144. doi:10.1001/archpsyc.58.12.1137

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., . . . Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ, 372*, n71. doi:10.1136/bmj.n71

Palmier-Claus, J. E., Dunn, G., & Lewis, S. W. (2012). Emotional and symptomatic reactivity to stress in individuals at ultra-high risk of developing psychosis. *Psychological medicine, 42*(5), 1003-1012. doi:10.1017/S0033291711001929

Palmier-Claus, J. E., Dunn, G., Taylor, H., Morrison, A., & Lewis, S. (2013). Cognitive-self consciousness and metacognitive beliefs: Stress sensitization in individuals at ultra-high risk of developing psychosis. *British Journal of Clinical Psychology, 52*(1), 26-41.

Peterson, R. A., & Brown, S. P. (2005). On the Use of Beta Coefficients in Meta-Analysis. *Journal of applied psychology, 90*(1), 175-181. doi:10.1037/0021-9010.90.1.175

Pluye, P., Gagnon, M. P., Griffiths, F., & Johnson-Lafleur, J. (2009). A scoring system for appraising mixed methods research, and concomitantly appraising qualitative, quantitative and mixed methods primary studies in Mixed Studies Reviews. *International Journal of Nursing Studies, 46*(4), 529-546. doi:10.1016/j.ijnurstu.2009.01.009

Pos, K., de Wit, I. E., van Dijk, F. A., Bartels-Velthuis, A. A., Bruggeman, R., Meijer, C. J., . . . van Winkel, R. (2017). An experience sampling study on the ecological validity of the SWN-20: Indication that subjective well-being is associated with momentary affective states above and beyond psychosis susceptibility. *Psychiatry Research, 258*(()), 234-238. doi:10.1016/j.psychres.2017.08.017

Rauschenberg, C., van Os, J., Cremers, D., Goedhart, M., Schieveld, J. N. M., & Reininghaus, U. (2017). Stress sensitivity as a putative mechanism linking childhood trauma and psychopathology in youth's daily life. *Acta Psychiatrica Scandinavica, 136*(4), 373-388. doi:10.1111/acps.12775

Read, J., van Os, J., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica, 112*(5), 330-350. doi:10.1111/j.1600-0447.2005.00634.x

Reininghaus, U., Gayer-Anderson, C., Valmaggia, L., Kempton, M. J., Calem, M., Onyejiaka, A., . . . Morgan, C. (2016). Psychological processes underlying the association between childhood trauma and psychosis in daily life: an experience sampling study. *Psychological Medicine, 46*(13), 2799-2813. doi:10.1017/S003329171600146X

Reininghaus, U., Kempton, M. J., Valmaggia, L., Craig, T. K. J., Garety, P., Onyejiaka, A., . . . Morgan, C. (2016). Stress sensitivity, aberrant salience, and threat anticipation in early psychosis: An experience sampling study. *Schizophrenia Bulletin, 42*(3), 712-722. doi:10.1093/schbul/sbv190

Rössler, W., Ajdacic-Gross, V., Rodgers, S., Haker, H., & Müller, M. (2016). Childhood trauma as a risk factor for the onset of subclinical psychotic experiences: Exploring the mediating effect of stress sensitivity in a cross-sectional epidemiological community study. *Schizophrenia Research, 172*(1-3), 46-53. doi:10.1016/j.schres.2016.02.006

Ruzibiza, C., Grattan, R. E., Eder, R., & Linscott, R. J. (2018). Components of schizophrenia liability are not uniformly associated with stress sensitivity, resilience, and coping. *Psychiatry Research, 260*, 10-16. doi:10.1016/j.psychres.2017.11.039

Söder, E., Krkovic, K., & Lincoln, T. M. (2020). The relevance of chronic stress for the acute stress reaction in people at elevated risk for psychosis. *Psychoneuroendocrinology, 119*, 104684-104684. doi:10.1016/j.psyneuen.2020.104684

Tessner, K. D., Mittal, V., & Walker, E. F. (2011). Longitudinal study of stressful life events and daily stressors among adolescents at high risk for psychotic disorders. *Schizophrenia Bulletin, 37*(2), 432-441.

Trotman, H. D., Holtzman, C. W., Walker, E. F., Addington, J. M., Bearden, C. E., Cadenhead, K. S., . . . McGlashan, T. H. (2014). Stress exposure and sensitivity in the clinical high-risk syndrome: Initial findings from the North American Prodrome Longitudinal Study (NAPLS). *Schizophrenia Research, 160*(1), 104-109. doi:10.1016/j.schres.2014.09.017

Udachina, A., Bentall, R. P., Varese, F., & Rowse, G. (2017). Stress sensitivity in paranoia: poor-me paranoia protects against the unpleasant effects of social stress. *Psychological Medicine, 47*(16), 2834-2843. doi:10.1017/S0033291717001362

Vaessen, T., van Nierop, M., Decoster, J., Delespaul, P., Derom, C., de Hert, M., . . . Myin-Germeys, I. (2017). Is sensitivity to daily stress predictive of onset or persistence of psychopathology? *European psychiatry, 45*, 167-173. doi:10.1016/j.eurpsy.2017.07.002

Vaessen, T., Viechtbauer, W., van der Steen, Y., Gayer-Anderson, C., Kempton, M. J., Valmaggia, L., . . . Myin-Germeys, I. (2019). Recovery from daily-life stressors in early and chronic psychosis. *Schizophrenia Research, 213*, 32-39. doi:10.1016/j.schres.2019.03.011

van der Steen, Y., Gimpel-Drees, J., Lataster, T., Viechtbauer, W., Simons, C., Lardinois, M., . . . Wagner, M. (2017). Clinical high risk for psychosis: the association between momentary stress, affective and psychotic symptoms. *Acta Psychiatrica Scandinavica, 136*(1), 63-73.

van Nierop, M., Lecei, A., Myin-Germeys, I., Collip, D., Viechtbauer, W., Jacobs, N., . . . van Winkel, R. (2018). Stress reactivity links childhood trauma exposure to an admixture of depressive, anxiety, and psychosis symptoms. *Psychiatry Research, 260*, 451-457.

van Winkel, R., Stefanis, N. C., & Myin-Germeys, I. (2008). Psychosocial Stress and Psychosis. A Review of the Neurobiological Mechanisms and the Evidence for Gene-Stress Interaction. *Schizophrenia Bulletin, 34*(6), 1095-1105. doi:10.1093/schbul/sbn101

Varese, F., Smeets, F., kker, M., Lieverse, R., Lataster, T., Viechtbauer, W., . . . 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. doi:10.1093/schbul/sbs050

Veling, W., Counotte, J., Pot-Kolder, R., Van Os, J., & Van Der Gaag, M. (2016). Childhood trauma, psychosis liability and social stress reactivity: a virtual reality study. *Psychological Medicine, 46*(16), 3339-3348.

Veling, W., Pot-Kolder, R., Counotte, J., van Os, J., & van der Gaag, M. (2016). Environmental social stress, paranoia and psychosis liability: a virtual reality study. *Schizophrenia Bulletin, 42*(6), 1363-1371.

Vignaud, P., Reilly, K. T., Donde, C., Haesebaert, F., & Brunelin, J. (2019). Clinical effects of mindfulness-based intervention in patients with first episode psychosis and in individuals with ultra-high risk for transition to psychosis: a review. *Frontiers in psychiatry, 10*(797), 1-9.

Westermann, S., Grezellschak, S., Oravecz, Z., Moritz, S., Lüdtke, T., & Jansen, A. (2017). Untangling the complex relationships between symptoms of schizophrenia and emotion dynamics in daily life: Findings from an experience sampling pilot study. *Psychiatry Research, 257*, 514-518. doi:10.1016/j.psychres.2017.08.023

Wichers, M., Schrijvers, D., Geschwind, N., Jacobs, N., Myin-Germeys, I., Thiery, E., . . . van Os, J. (2008). Mechanisms of gene–environment interactions in depression: evidence that genes potentiate multiple sources of adversity. *Psychological Medicine, 39*(7), 1077-1086. doi:10.1017/S0033291708004388

Table 1.
Overview of studies included in the review and quality assessment.

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Experience Sampling Method (ESM)								
Booij et al. (2018), The Netherlands	ESM	411 General population	Activity-related stress and social-interaction stress in relation to positive and negative affect.	Subclinical psychotic experiences were measured using the CAPE.	No significant interaction effects found between the daily stress measure and psychotic experiences in predicting positive or negative affect.	↔	Quantitative non-randomised	100%
Chun et al. (2017), Spain	ESM	206 Undergraduate students	Social stress and stressfulness of situation in relation to negative affect	Diagnostic interviews including the structures clinical interview for DSM-IV Axis II disorders, schizotypal, schizoid and paranoid personality disorder modules.	In high stress situations, those with higher levels of positive schizotypy experienced greater negative affect and those with high negative schizotypy experienced less negative affect.	In high stress: ↑ for positive schizotypy, ↓ for negative schizotypy	Quantitative non-randomised	60%
Collip, Nicolson, et al. (2011), The Netherlands	ESM	60 siblings of individuals with psychosis, 63 CON	Event-related stress in relation to negative affect.	Trait psychosis liability measured by CAPE.	No difference between siblings and CON in level of emotional stress reactivity.	↔	Quantitative non-randomised	100%
Collip, Wigman, et al. (2013), Belgium	ESM	467 with lower psychosis vulnerability, 62 with higher psychosis vulnerability	Activity-related stress, event-related stress and social stress in relation to negative affect and positive affect.	CAPE	Individuals with persistent subclinical psychosis symptoms showed more negative affect in response to event, activity and social stress and less positive affect in response to activity stress than those with low subclinical symptoms.	↑	Quantitative non-randomised	100%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Frissen et al. (2014), The Netherlands	ESM	57 PSY, 59 relatives, 75 CON	Event-related stress in relation to negative affect.	n/a	The association between stress sensitivity and negative affect was higher for PSY group, than relatives and CON.	↑ PSY > CON and relatives	Quantitative non-randomised	100%
Habets et al. (2012), The Netherlands	ESM	20 PSY, 37 siblings of individuals with psychotic disorder, 32 CON *Overlapping PSY sample with Lataster et al. (2010)	Event-related stress and social stress in relation to negative affect	PANSS	Individuals with psychosis had higher emotional stress reactivity than controls and siblings, in relation to event-related stress.	Event-related stress: ↑ PSY > CON and relatives Social Stress: ↔	Quantitative non-randomised	80%
Kramer et al. (2014), Belgium	ESM	515 General population twin sisters	Event-related stress in relation to negative affect.	Feelings of paranoia measured through ESM, SCL-90-R and CAPE.	Stress sensitivity positively moderated the effect of an increase of negative affect on paranoia levels.	↑	Quantitative descriptive	80%
Lataster et al. (2010), The Netherlands and Belgium	ESM	72 PSY, 80 siblings	Event-related stress and activity-related stress in relation to negative affect.	CASH	Higher stress reactivity was found in PSY compared to siblings. Higher stress reactivity was found in siblings with high and intermediate scores on positive symptoms compared to PSY with low scores on positive symptoms.	↑	Quantitative non-randomised	80%
Lataster et al. (2013), The Netherlands and Belgium	ESM	64 PSY *Overlapping PSY sample with Habets et al. (2012)	Event-related stress in relation to negative affect.	PANSS, CASH and ESM	Current and lifetime positive symptoms positively moderated the association between stressful events and negative affect. There was a negative interaction effect for current negative symptoms and no interaction effect for lifetime negative symptoms.	↑ for positive symptoms ↓ for negative symptoms	Quantitative descriptive	100%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Lataster et al. (2009), Belgium	ESM	535 General population twin sisters	Event-related stress and activity-related stress in relation to negative affect.	CAPE	Increased vulnerability to psychosis was associated with increased emotional stress reactivity.	↑	Quantitative descriptive	100%
Myin-Germeys et al. (2001), The Netherlands	ESM	42 PSY, 47 first-degree relatives, 49 CON *Same PSY and CON samples as Myin-Germeys, Peeters, et al. (2003) and Glaser, Os, Mengelers, and Myin-Germeys (2008)	Event-related stress, activity-related stress, social-stress and thought-related stress in relation to negative and positive affect.	n/a	Greater increase in negative affect and decrease in positive affect in PSY compared to controls in several measures of stress, and relatives, on fewer stress measures. Authors state that relatives reported greater increase in negative affect to stress than controls.	↑ PSY > CON and relatives	Quantitative non-randomised	80%
Palmier-Claus et al. (2012), UK	ESM	27 PSY, 27 UHR, 27 CON *Same UHR sample at Palmier-Claus, Dunn, Taylor, Morrison, and Lewis (2013)	Event-related stress, activity-related stress and social-stress in relation to negative affect.	n/a	UHR experienced greater negative affect in response to activity-related and social stress compared to PSY and CON. There was no significant difference between CON and PSY. No additional outcome of interest in Palmier-Claus et al. (2013).	Activity-related and social stress: UHR > PSY and CON CON=PSY	Quantitative non-randomised	80%
Pos et al. (2017), The Netherlands	ESM	63 PSY, 61 siblings of individuals with psychotic disorder	Negatively appraised events in relation to negative affect.	n/a	PSY group experienced higher negative affect in relation to negatively appraised events compared to siblings.	↑	Quantitative non-randomised	60%
Rauschenberg et al. (2017), The Netherlands	ESM	43 service users accessing mental health services, 16 siblings of service users and 40 CON Adolescents to young adults	Event-related, activity-related and social stress in relation to negative affect.	CAPE	Negative affect in relation to activity-related stress was higher in service users compared to siblings and higher in controls compared to siblings.	Event and activity-related: Service users > siblings, Activity-related: controls > siblings Social stress: ↔	Quantitative non-randomised	100%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Reininghaus, Kempton, et al. (2016), UK *Combined with Klippel et al. (2017) and Reininghaus, Gayer-Anderson, et al. (2016)	ESM	51 PSY, 46 At-risk Mental State, 53 CON	Event-related, activity-related and social stress in relation to negative affect.	Psychotic experiences measured through ESM.	Higher emotional stress reactivity in at-risk mental state and PSY compared to controls. Higher emotional stress reactivity in at-risk mental state than PSY. Stress reactivity was associated with more intense psychotic experiences. The indirect effect of activity-related stress to psychotic experiences via negative affect was greater in ARMS than controls.	ARMS and PSY > CON ARMS > PSY	Quantitative non-randomised	100%
Udachina, Bentall, Varese, and Rowse (2017), UK	ESM	91 PSY (grouped by remitted paranoia, paranoia and high deservedness (bad-me) and paranoia and low deservedness (poor-me)), 52 CON	Activity-related and social stress in relation to negative and positive affect.	n/a	Negative affect in relation to social stress was higher in bad-me group compared to all other groups. Negative affect in relation to activity-related stress was higher in poor-me group compared to CON. Whereas, the poor-me group experienced less decrease in positive affect compared to all other groups and the decrease in positive affect due to activity-stress was smaller in the bad-me group compared to all others. Decrease in positive affect was greater in controls than remitted patients.	Mixed	Quantitative non-randomised	60%
Vaessen et al. (2017), The Netherlands	ESM	445 General population (adolescents and young adult twins and siblings)	Event-related stress in relation to negative affect.	SCL-90 (at baseline and 1 year follow-up)	Emotional stress reactivity at baseline was not associated with follow-up psychotic symptoms. However, emotional reactivity to small stressors was related to follow-up symptoms in those with higher baseline symptoms.	Stress reactivity at baseline: ↔ Emotional reactivity to small stressors: ↑	Quantitative descriptive	80%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Vaessen et al. (2019), The Netherlands	ESM	162 Chronic psychosis, 127 Early psychosis (UHR), 220 CON *Combined participant data from other studies	Event-related stress in relation to negative affect.	n/a	No difference between CON and chronic psychosis in initial emotional reactivity to stress. There was greater initial reactivity to daily stressors in early psychosis compared to chronic psychosis.	Chronic psychosis and CON ↔	Quantitative non-randomised	80%
van der Steen et al. (2017), Germany, The Netherlands & Belgium	ESM	24 PSY, 22 CHR, 26 CON	Event-related stress, activity-related stress and social-stress in relation to negative affect.	n/a	The CHR group experienced more negative affect in relation to activity-related stress than PSY group and the PSY group experienced higher levels than controls. There was no significant differences for event-related and social stress.	Activity-related stress: CHR > PSY PSY > CON Event-related and social stress: ↔	Quantitative non-randomised	100%
van Winkel et al. (2008), The Netherlands	ESM	31 PSY cannabis users, 25 non-psychotic cannabis users	Event-related stress in relation to negative and positive affect.	n/a	The psychosis group had greater increase in negative affect in response to stress than controls.	↑	Quantitative non-randomised	60%
Westermann et al. (2017), Germany	ESM	15 PSY	Momentary emotional state and feelings.	CAPE	Positive symptoms of psychosis were not associated with stress sensitivity.	↔	Quantitative non-randomised	80%
Cross-sectional								
Cullen et al. (2014), UK	Cross-sectional	42 typically developing low-risk children, 29 children at higher risk of schizophrenia due to antecedents, 19 children with family history of schizophrenia, 5 children with multiple antecedents and family history.	7-item questionnaire, adapted from Heubeck and O'Sullivan (1998), which measured daily stressors and how distressed each event made them feel.	n/a	Children with family history of schizophrenia or who are at higher risk due to multiple antecedents linked to schizophrenia, experienced greater distress from daily stressor than typically developing children (d = 0.53 – 0.63).	↑	Quantitative non-randomised	100%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
DeVylder et al. (2013), USA	Cross-sectional	65 CHR, 24 CON Adolescents to young adults	Impaired tolerance to stress measured on the SOPS	n/a	Greater impaired tolerance to stress in CHR than CON (d = 1.48). There was no correlation between psychotic symptoms and impaired tolerance to stress.	↑	Quantitative non-randomised	100%
DeVylder and Hilimire (2015), USA	Cross-sectional	Undergraduate students 161 who experience auditory hallucination, 461 who do not experience auditory hallucinations.	Psychological Stress Index	n/a	Individuals who experience hallucinations reported higher stress sensitivity compared with those who did not experience hallucinations (d = 0.35).	↑	Quantitative non-randomised	80%
Gibson et al. (2014), USA	Cross-sectional	671 Undergraduate students	Perceived Stress Scale	92 item Prodromal Questionnaire (Loewy, Johnson, & Cannon, 2007).	Scores on measure of stress sensitivity positively correlated with attenuated positive psychotic symptoms (d = 0.61).	↑	Quantitative descriptive	60%
Gibson et al. (2019), USA	Cross-sectional	945 Undergraduate students	Perceived Stress Scale	92 item Prodromal Questionnaire (Loewy et al., 2007).	Scores on measure of stress sensitivity positively correlated with psychotic-like experiences (d = 0.95).	↑	Quantitative descriptive	80%
Grattan and Linscott (2019), New Zealand	Cross-sectional	184 Undergraduate students	Acute Hassles Scale	SPQ	Aspects of schizophrenia liability were associated with higher stress sensitivity at baseline (d = 0.47-0.80).	↑	Quantitative descriptive	100%
Laloyaux et al. (2016), Switzerland	Cross-sectional	112 General population	Short version of Perceived Stress Scale	Attenuated psychotic symptoms measured by SPQ, Launay–Slade Hallucinations Scale and Peters Delusions Inventory.	Stress sensitivity was positively associated with attenuated psychotic symptoms (d = 0.43-0.98)	↑	Quantitative descriptive	80%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Moskow et al. (2016)	Cross-sectional	93 CON and 348 CHR adolescents	Daily stress inventory including rating of how stressful each hassle was experienced.	SOPS	Higher scores on the daily stress inventory in CHR compared to CON.	↑	Quantitative non-randomised	80%
Rössler et al. (2016), Switzerland	Cross-sectional	403 General population grouped based on levels of subclinical psychosis symptoms	Perceived Stress Scale, PANAS and Screening Scale for Chronic Stress; scores were combined to measure stress sensitivity.	The Structured Interview for Assessing Perceptual Anomalies, the German version of the brief form of the SPQ (Klein, Andresen, & Jahn, 1997), the Paranoia Checklist, two psychosis subscales were derived from the SCL-90-R and the Creative experiences questionnaire as a measure of fantasy proneness.	Those with lower than average levels of subclinical psychotic symptoms scored lower on stress sensitivity compared to the groups with higher levels of subclinical symptoms. The group with only higher levels of anomalous experiences scored lower on stress sensitivity compared to those experiencing higher odd behaviours and beliefs and both odd behaviours and beliefs and anomalous experiences.	↑	Quantitative non-randomised	80%
Ruzibiza et al. (2018), New Zealand	Cross-sectional	230 Undergraduate students	Acute Hassles Scale (reactivity to stressors rated on severity scale)	SPQ measured schizophrenia liability	Higher levels of schizophrenia liability were associated with higher stress sensitivity as measured by the Acute Hassles Scale (d =0.43 – 0.93).	↑	Quantitative descriptive	80%
Tessner et al. (2011), USA	Cross-sectional	36 Schizotypal Personality Disorder, 42 Other Personality Disorders, 52 CON Adolescents	Daily stress inventory including rating of how stressful each hassle was experienced.	SOPS	Those with schizotypal personality disorders experienced greater distress in relation to daily stressors than those with other personality disorders and CON.	↑	Quantitative non-randomised	100%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Trotman et al. (2014), USA	Cross-sectional	314 CHR, 162 CON Adolescents to young adults	Daily stress inventory and rating of how stressful each hassle was experienced.	SOPS	CHR group experienced more subjective stress in response to daily hassles than CON (d = 0.54). Those who went on to develop psychosis had higher stress to daily hassles at baseline compared to those who stayed in prodromal stages and those who remitted (d = 0.33 and 0.74, respectively).	↑	Quantitative non-randomised	80%
Experimental								
Dinzeo et al. (2008), USA	Experimental stress paradigm	58 PSY, 21 CON	Negative affect measured, using PANAS, following a stress/challenge paradigm	BPRS -Expanded Version	No analysis was conducted on the data as part of the study. Data was shared and analysis showed no significant difference in change in negative affect between individuals with psychosis and controls.	↔	Quantitative non-randomised	80%
Horan and Blanchard (2003), USA	Experimental stress paradigm	36 PSY, 15 CON	36-item self-report questionnaire on positive and negative mood before and after role-play test.	BPRS	When comparing before and after the stress task, there was no difference between PSY and controls in negative or positive affect.	↔	Quantitative non-randomised	80%
Jongeneel et al. (2018), The Netherlands	Experimental stress paradigm	75 with higher psychosis liability (UHR and PSY) and 94 with lower psychosis liability (siblings and CON)	Subjective distress score before and after virtual reality social stress situation. Stress reactivity was measured by subjective distress during the experiment minus subjective distress before.	n/a	The higher liability psychosis group had higher stress reactivity scores compared to the lower psychosis liability group (d=0.43).	↑	Quantitative non-randomised	80%

Author, date, country	Design	Sample	Measure of emotional stress reactivity	Measure of psychotic symptoms	Main (relevant) findings	Direction of effect	Section of M-MAT	% score
Lincoln, Köther, et al. (2015), Germany	Experimental stress paradigm	35 PSY, 29 attenuated psychotic positive symptoms, 26 first-degree relatives, 28 CON *Same PSY and CON samples as Lincoln, Hartmann, et al. (2015)	Subjective stress ratings before and after noise stress, social stress and no stress conditions.	PANSS	Across conditions, the PSY group felt more stressed than relatives, those with attenuated psychotic symptoms and CON. There was a greater increase in stress response from the no stress condition to the noise stress condition in the PSY group compared to CON (d = 0.52). No additional outcome of interest in Lincoln, Hartmann, et al. (2015).	↑	Quantitative non-randomised	100%
Söder et al. (2020), Germany	Experimental stress paradigm	32 first-degree relatives and 43 CHR and 35 CON	Subjective stress and negative affect ratings before and after the Trier Social Stress Test	CAPE	No differences in subjective stress between groups. Higher negative affect for CHR compared with CON.	Subjective stress: ↔ Negative affect: ↑	Quantitative non-randomised	80%
Veling, Pot-Kolder, et al. (2016), The Netherlands	Experimental stress paradigm	High psychosis liability (55 PSY, 20 UHR), and low liability (42 Siblings, 53 CON) *Same participant data as Veling, Counotte, et al. (2016)	Maximum subjective distress rated after experiment	CAPE	There was greater subjective distress in response to stressors for those with high psychosis liability compared to low.	↑	Quantitative non-randomised	100%

ESM = Experience Sampling Method; PSY = Individuals with psychosis; CON =.Healthy Controls; CHR = Clinical High Risk of Psychosis; UHR = Ultra High Risk of Psychosis; CAPE = Community Assessment of Psychic Experiences; BPRS = Brief Psychiatric Rating Scale; PANSS = Positive and Negative Syndrome Scale; SCL-90-R = Symptom Checklist-90-Revised; SPQ = Schizotypal Personality Questionnaire; CASH = Comprehensive Assessment of Symptoms and History; SOPS = Scale of Prodromal Symptoms; PANAS = Positive and Negative Affect Schedule.

Direction of effect: ↑ greater psychotic experiences or psychosis vulnerability linked with higher ESR; ↔ equivocal; ↓ fewer psychotic experiences or lower psychosis vulnerability linked with higher ESR; > emotional stress reactivity is greater than; > less than.

Table 2.
Quality assessment for quantitative non-randomised studies.

Author	3.1	3.2	3.3	3.4	3.5
Booij et al (2018)	+	+	+	+	+
Chun et al (2017)	+	+	-	?	+
Collip et al (2011)	+	+	+	+	+
Collip et al (2013)	+	+	+	+	+
Cullen et al (2014)	+	+	+	+	+
Devylder et al (2013)	+	+	+	+	+
Devylder & Hillmire (2015)	+	-	+	+	+
Dinzeo et al (2008)	+	+	?	+	+
Frissen et al (2014)	+	+	+	+	+
Glaser et al (2008)	+	+	+	+	+
Habets et al (2012)	+	+	?	+	+
Horan & Blanchard (2003)	+	+	?	+	+
Jongeneel et al (2018)	+	+	?	+	+
Klippel et al (2017)	+	+	+	+	+
Lataster et al (2010)	+	+	-	+	+
Lincoln, Köther et al (2015)	+	+	+	+	+
Lincoln, Hartmann et al (2015)	+	+	+	+	+
Moskow et al (2016)	+	+	-	+	+
Myin-Germeys et al (2001)	+	+	+	-	+
Myin-Germeys et al (2003)	+	+	+	+	+
Palmier-Claus et al (2012)	+	+	-	+	+
Pos et al (2017)	+	+	-	-	+
Rauschenberg et al (2016)	+	+	+	+	+
Reininghaus et al (2016)	+	+	+	+	+
Rössler et al (2016)	+	+	?	+	+
Söder et al (2020)	+	+	+	-	+
Tessner et al (2011)	+	+	+	+	+
Trotman et al (2014)	+	+	?	+	+
Udachina et al (2017)	-	+	-	+	+
Vaessen et al (2019)	-	+	-	+	+
Van der Steen et al (2017)	+	+	+	+	+
Van Winkel et al (2008)	-	+	+	-	+
Veiling et al (2016)	+	+	+	+	+
Westermann et al (2017)	+	?	+	+	+

+ = the study met the criteria, ? = unclear if the study met the criteria, - = the study did not meet the criteria. 3.1. Are the participants representative of the target population? 3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)? 3.3. Are there complete outcome data? 3.4. Are the confounders accounted for in the design and analysis? 3.5. During the study period, is the intervention administered (or exposure occurred) as intended?

Table 3.
Quality assessment for quantitative descriptive studies.

Author	4.1	4.2	4.3	4.4	4.5
Gibson et al (2014)	+	?	+	?	+
Gibson et al (2019)	+	+	+	?	+
Grattan & Linscott (2019)	+	+	+	+	+
Kramer et al (2014)	?	+	+	+	+
Laloyaux et al (2016)	+	+	+	?	+
Lataster et al (2013)	+	+	+	+	+
Lataster et al (2009)	+	+	+	+	+
Palmier-Claus et al (2013)	+	+	+	-	+
Ruzibiza et al (2018)	+	-	+	+	+
Vaessen et al (2017)	+	+	+	-	+

4.1. Is the sampling strategy relevant to address the research question? 4.2. Is the sample representative of the target population? 4.3. Are the measurements appropriate? 4.4. Is the risk of nonresponse bias low? 4.5. Is the statistical analysis appropriate to answer the research question?

Appendix A

Critical Review of the Literature: Exact Search Terms

Applied Search to title, abstract and keywords as well as index terms

1. Psychosis
2. Psychotic
3. Schizophreni*
4. 1 OR 2 OR 3
5. Stress reactivity
6. Stress sensitivity
7. Sensitiv* NEAR/3 stress
8. React* NEAR/3 stress
9. 5 OR 6 OR 7 OR 8
10. 4 AND 9

PsychINFO (APA) Search

((((**Keywords**: (sensitiv* NEAR/3 stress)))) *OR*(((**abstract**: (sensitiv* NEAR/3 stress)))) *OR* (((**title**: (sensitiv* NEAR/3 stress)))) *OR* (((((**Keywords**: (react* NEAR/3 stress))))) *OR* ((((**abstract**: (react* NEAR/3 stress))))) *OR* ((((**title**: (react* NEAR/3 stress))))) *OR* ((((((**Keywords**: (stress-sensitivity)))))) *OR* (((((**abstract**: (stress-sensitivity)))))) *OR* (((((**title**: (stress-sensitivity)))))) *OR* (((((((**Keywords**: (stress-reactivity)))))))) *OR*((((((**abstract**: (stress-reactivity)))))))) *OR* ((((((**title**: (stress-reactivity)))))))))) *AND* ((((((**IndexTermsFilt**: ("Psychosis"))))) *OR*((((((**Keywords**: (psychosis))))) *OR* ((((**Keywords**: (psychotic)))))) *OR* (((((**abstract**: (psychosis))))) *OR* ((((**abstract**: (psychotic)))))) *OR* (((((**title**: (psychosis))))) *OR* ((((**title**: (psychotic)))))))) *OR*(((**IndexTermsFilt**: ("Schizophrenia")))) *OR* (**title**: (schizophreni*)) *OR* (**abstract**: (schizophreni*)) *OR* (**Keywords**: (schizophreni*)))

Appendix B: Missing Data for Systematic Literature Review

For the narrative synthesis, it was not possible to source the outcome of interest for the following studies:

- Collip, van Winkel, et al. (2011)
- Collip, Habets, et al. (2013)

For the meta-analysis, it was not possible to source additional data related to the outcome of interest to include the study in the analysis:

- Collip, Nicolson, et al. (2011)
- Lataster et al. (2010)
- Palmier-Claus et al. (2012)
- Habets et al. (2012)