**What can experimental studies tell us about paranoia and anxiety? A systematic review with implications for theory and clinical practice.**

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**What can experimental studies tell us about paranoia and anxiety? A systematic review with implications for theory and clinical practice.**

Background: Psychosis is one of the most disabling and costly long-term health conditions, and treatment outcomes remain modest. Interventions focused on specific symptoms, such as paranoia, show promise and typically target cognitive and behavioural maintenance processes. Anxiety is implicated in theories of paranoia; however, the nature of the relationship remains unclear. We review experimental studies of paranoia and anxiety against existing cognitive models.

Method: A systematic review strategy identified experimental studies assessing levels of anxiety and paranoia. Papers were assessed for quality, and data relating to samples, measures, designs and key findings were extracted and narratively synthesised.

Results: Nineteen studies met criteria for the review. Most found that manipulations impacting anxiety also impacted paranoia, with preliminary evidence for a causal relationship. The overall quality of the research was weak.

Conclusions: We recommend a research agenda to confirm initial evidence for the causal role of anxiety in increased paranoia, and whether targeting affect, in addition to cognitive and behavioural maintenance processes, improves outcomes in clinical groups and those at risk of psychosis.

Keywords: Paranoia; persecutory; anxiety; emotion; experimental; systematic review

# Introduction

Experimental evaluation of the psychological models underlying therapeutic interventions is necessary to test theoretical assumptions and ensure effective and ethical clinical practice. Cognitive-Behavioural Therapy (CBT) is an evidence-based treatment for psychosis (National Institute for Health & Care Excellence; NICE, 2014) based on current cognitive models (Garety et al., 2001; Morrison, 2001) that identify negative emotions (Garety et al., 2001; Freeman et al., 2002; Gumley et al., 2013; Kesting & Lincoln, 2013; Morrison, 2001), a deficit in skills regulating these emotions (Lincoln et al., 2015a,b), and negative beliefs about the self and/or others (Bentall et al., 1994; Freeman et al., 2002; Kesting & Lincoln, 2013) as crucial to the formation and maintenance of paranoia.

The threat-anticipation model by Freeman et al. (2002) proposes that persecutory delusions form by the interaction of three core processes (emotion and beliefs about the self, others and the world; anomalous experiences/ arousal; and cognitive biases) in response to a precipitant, for example, a significant life event or increased stress. This interaction initiates a search for meaning, and the consequent selection of an explanation results in the formation of a threat belief. The model proposes that in the formation of a persecutory delusion, pre-existing levels of anxiety influence beliefs about the self, others and the world that are activated in response to the precipitant.

Anxiety is considered the key emotion related to the onset of persecutory delusions (Freeman et al., 2002). The model predicts that paranoid ideation occurs in the presence of anxiety, that an increase in anxiety increases paranoid ideation, and that any reduction in anxiety could result in a reduction of paranoid ideation. A further prediction of the model is that anxiety mediates the effect of any single manipulation (i.e. precipitant) on the presence of paranoid ideation.

In clinical samples, deficits in the ability to regulate anxiety and depression have been associated with paranoia (Lincoln et al., 2015a,b). These align with interpersonal threat beliefs and particular processing patterns characteristic of persecutory delusions (e.g. ‘jumping to conclusions’), the most severe form of paranoia (Freeman et al., 2002; Garety et al., 2001).

There is also growing evidence that people with psychosis may be more sensitive to affective stimuli; this population show higher levels of stress sensitivity (Khoury & Lecomte, 2012; Llerena et al., 2012), threat anticipation (Reininghaus et al., 2016), and are less able to tolerate distress (Nugent et al., 2014), compared with healthy controls. However, recommended therapies typically prioritise cognitive and behavioural processes and fail to target emotion directly (Gumley et al., 2013).

## Previous systematic reviews

Previous reviews have investigated the role of anxiety and depression (Hartley et al., 2013) on the one hand, and self-beliefs and evaluations (Kesting & Lincoln, 2013; Tiernan et al., 2014) in psychotic experiences on the other. Key findings included the association of psychosis symptoms with affect (Hartley et al., 2013), negative self-concepts (Tiernan et al., 2014), unstable self-esteem and negative self-representations (Kesting & Lincoln, 2013). Taken together, these reviews support the maintaining factors proposed in Freeman et al.’s (2002) model, although the nature of the relationships between processes has not been systematically demonstrated. Most studies were cross-sectional or correlational in design and particular symptoms have not been explored, precluding conclusions regarding anxiety and depression in paranoia or persecutory delusions specifically. Furthermore, Hartley et al. (2013) did not conform to systematic review guidelines.

***The current review***

The aim of this review was to synthesise the experimental literature investigating paranoid ideation and anxiety, in order to ascertain causal relationships between key variables proposed by current cognitive models, with a view to informing both theoretical understanding and clinical practice. An exclusive focus on experimental studies is justified by the intention to explore causal relationships between variables, which can uniquely be derived from experimental designs (Kesting et al., 2013). The centrality of anxiety in the threat-anticipation model of persecutory delusions in particular, provides the rationale for focusing exclusively on the relationship between anxiety and paranoia (Freeman et al., 2002; Garety et al., 2001; Gumley et al., 2013; Morrison, 2001). The review includes studies of clinical and non-clinical samples based on the continuity hypothesis (van Os & Verdoux, 2002) and on the hierarchical model of paranoia (Freeman et al., 2005), both of which assume that psychotic symptoms such as paranoia occur across the population and posit that research in non-clinical populations can inform our understanding of clinical levels of symptomology (Freeman, 2007; van Os & Verdoux, 2002).

**Materials and method**

***Search strategy***

We completed a systematic review of the literature, following PRISMA guidelines (Moher et al., 2009). Search terms were entered into PsycINFO, MEDLINE, CINAHL Plus with Full Text, PsycARTICLES (via EBSCOhost) and Web of ScienceTM, applied to titles, abstracts and keywords. Included articles were published up to end November 2019.

Search terms were entered as three grouped concepts (A, B and C). Search terms A targeted anxiety ("anxiety" OR "fear" OR "worry" OR "stress"; identified by the use of the PsychInfo Thesaurus feature). Search terms B targeted paranoia ("paranoi\*" OR "delus\*" OR "delud\*" OR "persecut\*" OR "suspicious\*" OR “schizotypy”), following the Kesting and Lincoln (2013) review, with the addition of “schizotypy” to ensure broad inclusion of paranoia related studies. Search term C targeted study design ("experiment\*"). Search terms A, B and C were entered using the Boolean phrase “AND”.

***Inclusion and exclusion criteria***

*Inclusion criteria:*

1. An experimental study, defined as a quantitative study in which at least one

variable is manipulated with a minimum of two levels.

1. Anxiety and paranoia measured independently both before and after

experimental manipulation. Anxiety measures were identified if the scale or subscale included any word from search terms A. Paranoia measures were included if the scale measured paranoia, paranoid ideation, suspiciousness or persecutory delusions.

*Exclusion criteria:*

1. A single level of manipulation.
2. Anxiety and/or paranoia measured only once.
3. Anxiety and/or paranoia not analysed as independent constructs.
4. Neurological, neuroimaging or physiological studies with no psychological

measures of anxiety and paranoia.

1. Drug interventions.

Ambiguities regarding inclusion were resolved through discussion between the first and last authors.

***Selection process***

Search results were combined and duplicates removed. Titles and abstracts were screened for relevance, and excluded where (a) the abstract did not include any of search terms B, (b) a delusion was not specified as paranoid or specified as another type (e.g. grandiose), (c) suspiciousness was identified but did not refer to a psychological process or state (e.g. “a suspicious tumour”) or (d) the term “paranoid” served as an acronym for an unrelated concept. All remaining articles were then screened against the inclusion and exclusion criteria. Figure 1 illustrates the search and selection process (following Moher et al., 2009).

Figure 1 here

***Quality assessment***

The Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies (EPHPP QAT; Thomas et al., 2004) and linked dictionary ([www.ephpp.ca](http://www.ephpp.ca)) were utilised for quality assessment. Studies are rated using a scale of 1 (strong) to 3 (weak) across six domains (selection bias, study design, confounders, blinding, data collection method and withdrawals and dropouts), with a score of one weak rating yielding a global score of “Moderate” and two or more domain scores as weak yielding a global score of “Weak”. Validity and reliability reporting was only rated “Yes” if these were reported for >50% of the measures. All ratings were conducted by the first author with consultation with the third author in the case of ambiguity.

***Data extraction***

We extracted details of design, measurement and key findings from all included studies. Missing effect sizes were calculated where sufficient information was provided, following Thalhiemer and Cook (2002; t-tests and F-tests), www.psychometrica.de/effect\_size.html#dep (chi-square), or Cohen (1992) (multiple regression). Effect sizes were interpreted following Cohen (1992) (*d*, *r*, *η²*, ƒ²) and Kinnear and Gray (2008) (*ηp*²). Insufficient homogeneity of participants, intervention, outcomes and effects precluded a meta-analysis (Brown & Richardson, 2017). A narrative synthesis of the results is presented below.

**Results**

Nineteen studies met criteria for the review. Design and measurement details are presented in Table 1. Key results are presented in Table 2.

Table 1 here

***Study methodology and analysis strategies***

Seven of the 19 studies (37%) recruited clinical samples. Table 1 illustrates considerable variation in design, experimental manipulation, and measures of paranoia and anxiety, across this body of literature. The analytic strategies permitted exploration of the direct effects of experimental manipulation on paranoia and anxiety, and some of the indirect predictive and mediation effects.

Table 2 here

***Direct effects of experimental manipulations on anxiety and paranoia***

Five of the seven studies using single episode manipulations found increases in anxiety and paranoia (Bullock et al., 2016; Casanova et al., 1988; Cowles & Hogg, 2019; Freeman et al., 2015; Isnanda et al., 2014). Two studies (Bullock et al., 2016; Newman-Taylor et al., 2018) found reductions in anxiety and paranoia post-manipulation. Bullock et al. (2016) and Newman-Taylor et al. (2018) found differential effects for pleasant and distressing imagery. A social comparison manipulation resulted in no change in either anxiety or paranoia (Ascone et al., 2017).

Multiple-episode manipulations varied in duration, target outcome and experimental manipulation. The majority of these tasks were designed to be beneficial, and resulted in reductions in anxiety and paranoia (Ameri et al., 2017; Franco et al.; 2010; Giusti et al., 2017; Hou et al., 2014; Passini et al., 1977; Pourmohamadreza-Tajrishi et al., 2015). Foster et al. (2010), and Garety et al. (2015) found differential effects for anxiety and paranoia. Reeve et al. (2018) found increases in both anxiety and paranoia. Effect sizes for changes in anxiety were larger than for paranoia in most studies investigating multiple-episode psychological manipulations (Franco et al., 2010; Giusti et al., 2017; Hou et al., 2014; Pourmohamadreza-Trajrishi et al., 2015; Reeve et al., 2018).

Three multiple-episode studies utilised physical manipulations (e.g. exercise regimes) and reported reductions in both outcomes, with small to large effect sizes (Müller et al., 2014; Talakoub et al., 2012; Xu et al., 2016).

***Predictive and mediation effects***

Cowles and Hogg (2019) showed that only negative affect was significant in predicting paranoia in a regression model, and Reeve et al. (2018) found increases in paranoia were largely mediated by negative affect (a composite measure of anxiety, depression and stress). Baseline symptomology was associated with intervention effects in two studies (Cowles & Hogg, 2019; Giusti et al., 2017) but not a third (Newman-Taylor et al., 2018). Freeman et al. (2015) found no significant mediation effect for anxiety or depression, and Garety et al. (2015) found no evidence for a mediation effect of cognitive variables on the intervention effect on paranoia.

***Quality review***

Despite strong ratings in certain domains of the quality assessment, every paper in the review received an overall rating of “weak”. Most commonly, the validity of the measures was not sufficiently reported.

**Discussion**

This review of the experimental literature examined the association between anxiety and paranoia to determine whether there is support for the hypothesis that anxiety plays a causal role in this relationship. Nineteen studies met inclusion criteria, most reporting changes in both constructs following experimental manipulation. One study found change in neither, and only two studies found change in just one of the two. Studies of the direct effects of experimental manipulations on anxiety and paranoia provide clear support for an associative relationship, in both non-clinical and clinical populations, and over single and multiple-episode experimental manipulations.

The few studies that allowed for exploration of causality (Cowles & Hogg, 2019; Freeman et al., 2015; Garety et al., 2015; Reeve et al., 2018) did not always explore anxiety as an independent construct in the regression analyses (though for inclusion, had analysed this independently from pre to post manipulation). Due to the scarcity of the evidence base and relevance to the cognitive models of paranoia, studies exploring the role of “negative affect” (a collapsed construct of anxiety and other forms of affect) were included in the final review. These suggested that negative affect, rather than anxiety specifically, contributes to changes in paranoia. While promising, evidence of a causal rather than associative role for anxiety is less robust due to the limited number of studies utilising these study designs and analysis strategies.

***Critique of the literature***

The literature to date, for both clinical and non-clinical samples, were biased by gender with an overrepresentation of females, limiting the generalizability of the results.

Experimental manipulations lacked consistency in duration, content, and design, considerably limiting the conclusions that can be drawn about which specific components have a causal effect on symptoms. Effect sizes and quality indicators were not consistently reported, and the array of assessment measures employed makes the results difficult to synthesise across studies. Most studies utilised a single dimension measure of paranoia, however those that employed multiple measures, at times with differing effects, suggest that dimensions of paranoia may be differentially sensitive to manipulations. Similarly, most anxiety measures were unidimensional, whereas the hierarchy model of paranoia (Freeman et al., 2005) suggests socially-related anxieties may be more relevant to the onset of paranoid symptoms.

***Future research agenda***

Experimental studies allow examination of causal relationships between variables (Kesting et al., 2013). The lack of rigorous research in this area is striking and limits conclusions that can be drawn about the relationship between anxiety and paranoia. This in turn limits the application or adaptation of well-evidenced interventions targeting anxiety for people with paranoia. In order to confirm preliminary evidence for the causal role of anxiety in increased paranoia, we recommend the following research priorities in clinical and analogue groups:

1. Replication of studies examining predictive and mediation effects of negative affect on paranoia.
2. Studies examining the impact of affect manipulation and affect regulation on paranoia. Physiological interventions showed preliminary promise in reducing anxiety and paranoia, and should be further explored to understand their impact.
3. Consistency in experimental manipulations – social stress, interpersonal imagery, exercise and therapeutic (e.g. CBT-based) tasks have all been shown to impact anxiety and paranoia.
4. Consistency in use of measures to assess key variables; together, the studies used 15 different measures of paranoia (most frequently he SCL-90-R paranoid ideation subscale, n=7) and 17 different measures of anxiety (most commonly the SCL-90-R anxiety subscale, n=7). Use of multidimensional measures of these constructs would permit further understanding of the specificity of effects, which could be extrapolated to theoretical models.
5. Reporting on quality indicators, including controlling for confounders, blinding assessors, reporting validity information for every measure, and accounting for withdrawals.

***Theoretical and clinical implications***

The continuity hypothesis (van Os & Verdoux, 2002) and hierarchical models (Freeman et al., 2005) were supported. Preliminary evidence for the causal role of affect supports the hypothesis that in vulnerable individuals, minor stressors trigger negative affect, which then increases likelihood of paranoia (Myin-Germeys & van Os, 2007), as predicted by existing cognitive models of paranoia (Freeman et al., 2002; Freeman, 2016; Gumley et al., 2013; Morrison, 2001). Taken together, these results suggest that both at risk and clinical groups would benefit from interventions targeting affect and affect regulation. This is supported by evidence that brief CBT for worry is effective in reducing paranoia in people with psychosis (Freeman et al., 2015), and a meta-analysis of CBT for anxiety in psychosis (Heavens et al., 2019). If people vulnerable to or presenting with psychosis can learn to manage emotional arousal, particularly in socially stressful environments, they may be less susceptible to increases in paranoia.

***Summary and conclusion***

This is the first systematic review of the experimental literature designed to examine the relationship between anxiety and paranoia. The results provide good evidence for an association between affect and paranoia in response to experimental manipulations, and preliminary evidence for the causal role of negative affect (as opposed to anxiety specifically) in paranoia, across both clinical and non-clinical groups. This suggests that interventions focused on affect and affect regulation may be effective in reducing paranoia. We recommend a research agenda designed to address the considerable variation in experimental methodology, and confirm whether targeting affect, in addition to cognitive and behavioural maintenance processes, improves outcomes in clinical groups and those at risk of psychosis.

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| **Table 1. Key features of the nineteen studies meeting inclusion criteria** | | | | | | | | | |
| **Study** | **Sample (N; clinical status¹; age²; country)** | **Design & manipulation**  **single (S)/ multiple (M)³** | **Control group (Y/N)4** | **Measures pre-manipulation** | | **Measures post-manipulation** | | **Analytic strategy** | **QAT rating** |
| Anxiety | Paranoia | Anxiety | Paranoia |
| Ameri, Vazifeshenas and Haghparast (2017) | N = 60; Non-clinical; > 60 years; Iran | 2x2 Audiobook workshops (M) | Y | Symptom Checklist (SCL-90-R; Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | T-tests | Weak |
| Ascone, Jaya and Lincoln (2017) | N = 172; Non-clinical; Not stated; Germany | 2x2  Social profile comparison (S) | N | Validated emotion intensity rating (VEIR) - Anxiety; Insecure Striving (Fears of Rejection and Losing Opportunities) | Paranoia checklist (PC; state) | VEIR- Anxiety | PC (state) | Repeated Measures (RM) ANOVA; Regression | Weak |
| Bullock, Newman-Taylor and Stopa (2016) | N = 30, Non-clinical; M = 20.9; UK | 2x2  Interpersonal imagery (S) | N | State and Trait Anxiety Inventory (STAI) | Paranoia Scale (PS); PC (state) | SAI | PC (state) | T-test and Chi Square; Mixed Model (MM) ANOVA + post-hoc t-test | Weak |
| Casanova, Katkovsky and Hershberger (1988) | N = 80; Non-clinical; M = Not stated; USA | 2x2x2  Feedback/ hearing (S) | N | SAI | Paranoid Adjective Checklist (PAC) | SAI | PAC | MANOVA + post-hoc ANOVA | Weak |
| Cowles and Hogg (2019) | N= 22; Clinical; M = 32.82; UK | 2x2  Memory recall | Y | Brief state measure (BMS; anxiety subscale) | PC (conviction subscale + state, adapted); Psychotic-Symptoms Rating Scale – B (PSYRATS; paranoia subscale) | BMS (anxiety subscale) | PC (state, adapted) | T-tests | Weak |
| Foster, Startup, Potts and Freeman (2010) | N = 20; Clinical; M = 39.55\*; UK | 2x3  Worry-based CBT (M) | Y | Penn State Worry Questionnaire (PSWQ) | Green et al. Paranoid Thoughts Scale (GPTS) | PSWQ | GPTS | Multilevel linear regression and Kendall Tau correlations | Weak |
| Franco, Mañas, Cangas, Moreno and Gallego (2010) | N = 68; Non-clinical; M = 40.2; Spain | 2x3  Mindfulness (M) | Y | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | T-tests | Weak |
| Freeman et al. (2015) | N = 59; Clinical; M = 43.35\*; UK | 2x2  Street exposure (S) | Y | Visual analogue scale (VAS)- Anxiety | State Social Paranoia Scale (SSPS); VAS - Paranoia and Conviction; Schizotypal Symptoms Inventory - Paranoia (SSI-P) | VAS- Anxiety | SSPS; VAS - Paranoia and Conviction; SSI- P | ITT ANCOVAs and causal mediation analysis | Weak |
| Garety et al. (2015) | N = 101; Clinical; M = 41.6; UK | 2x4  Computerized reasoning training (M) | Y | Beck Anxiety Inventory (BAI); VAS - Anxiety | GPTS (6 items + conviction) | VAS- Anxiety | GPTS (6 items + conviction) | ITT ANCOVA; Regression | Weak |
| Giusti et al. (2017) | N = 60; Clinical; M =; 25.45\*; Italy | 2x2x2  Anxiety management & metacognitive training (M) | Y | SCL-90-R (Anxiety and Phobic Anxiety); STAI; Self-Rating Anxiety Scale (SAS) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety and Phobic Anxiety); STAI; SAS | SCL-90-R (Paranoid Ideation) | ANOVA + Chi square; RM ANCOVA | Weak |
| Hou, Hu, Liang and Mo (2014) | N = 103; Non-clinical; M =; 53.45\*; China | 2x2  CBT (M) | Y | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | T-tests; Chi-square | Weak |
| Isnanda, Brinkman, Veling, van der Gaag and Neerincx (2014) | N = 24; Non-clinical; M = 28.42; The Netherlands | 2x2x2  Stress probability and cycle time (S) | N | Social Interaction Anxiety Scale (SIAS) | GPTS | Subjective Unit of Distress (SUD) - Anxiety | Coding Scheme Paranoid Thoughts Commentaries (CSPTC) | RM MM ANOVA | Weak |
| Müller, Haffelder, Schlotman, Schaefers and Teuchert-Noodt (2014) | N = 50; Clinical; M = 48.25; Germany | 2x4  Brain rhythm adapted music & exercise (M) | Y | Brief Symptoms Inventory (BSI; Anxiety and Phobic Anxiety) | BSI (Paranoid Ideation) | BSI (Anxiety and Phobic Anxiety) | BSI (Paranoid Ideation) | Chi-square | Weak |
| Newman-Taylor, Kemp, Potter and Au-Yeung (2018) | N = 301; Non-clinical; M = 20.1; UK | 2x2  Mental imagery (S) | N | STAI | PS; PC (state) | SAI | PC (state) | MM ANOVA and t-tests | Weak |
| Passini, Watson, Dehnel, Herder and Watkins (1977) | N = 50; Clinical; M = 43.8\*; USA | 2x2  Alpha wave biofeedback training (M) | Y | STAI; Brief Psychiatric Rating Scale (BPRS; Anxiety); Multiple Affect Adjective Check List (MAACL; Anxiety) | Minnesota Multiphasic Personality Inventory (MMPI; Paranoia); BPRS (Suspiciousness) | STAI; BPRS (Anxiety); MAACL (Anxiety) | MMPI (Paranoia); BPRS (Suspiciousness) | ANOVA | Weak |
| Pourmohamadreza-Tajrishi, Azadfallah, Hemmati Garakani and Bakhshi (2015) | N = 55; Non-clinical; M = 35.22; Iran | 2x2  Problem-focused coping (M) | Y | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | ANCOVA | Weak |
| Reeve, Emsley, Sheaves and Freeman (2018) | N = 68; Non-clinical; M = 22.5; UK | 2x2  Sleep loss | Y | DASS-42 (Anxiety); Worry Questionnaire | Specific Psychotic Experiences Questionnaire (SPEQ; Paranoia) | DASS-42 (Anxiety); Worry Questionnaire | SPEQ (Paranoia) | Multilevel modelling |  |
| Talakoub, Gorbani, Hasanpour, Zolaktaf and Amini (2012) | N = 64; Non-clinical; M = 17.47\*; Iran | 2x2  Aerobic exercise (M) | Y | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety and Phobic Anxiety) | SCL-90-R (Paranoid Ideation) | T-test | Weak |
| Xu, Li and Yao (2016) | N = 115; Non-clinical; M = 67.35; China | 2x2  Collective exercise (M) | Y | SCL-90-R (Anxiety) | SCL-90-R (Paranoid Ideation) | SCL-90-R (Anxiety) | SCL-90-R (Paranoid Ideation) | T-tests; Chi square and Willcoxon Signed Ranks | Weak |
| ¹ *Clinical defined as either (a) participants selected or included based on a psychiatric diagnosis and/or (b) participants recruited from a mental health/ psychiatric clinical setting. Participants selected on physical health diagnoses or recruited from physical health settings are considered non-clinical samples.*  ² *Asterixed means are pooled means calculated from group means provided in the article.*  ³ *Single episode manipulations refer to those studies in which the manipulation and assessments took place at a single timepoint; multiple episode refers to instances in which assessment and manipulation took place over a minimum of two separate time points.*  4 *Y = Yes; N = No* | | | | | | | | | |

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| **Table 2. Key findings from the nineteen studies meeting inclusion criteria** | |
| **Study** | **Key findings** |
| Ameri et al. (2017) | 1. Significant reduction in anxiety (*p* <.05), phobic anxiety (*p* <.05) and paranoid ideation (*p* <.05) in experimental group from pre to post-test. 2. Significant between-groups differences at post-test on anxiety (*p* < .05, *d* = 1.611; very large), phobic anxiety (*p* <.05, *d* = 2.141; very large) and paranoid ideation (*p* < .05 *d* = 2.291; very large); scores were significantly lower in the experimental group compared to the control group. |
| Ascone et al. (2017) | 1. No significant interaction effect for anxiety (*p* = .435, *η²*= 0.004) or paranoia (*p* = .381*, η²=* 0.005). 2. Post-test paranoia predicted by pre-test paranoia and groupXinsecure striving (*p* <.01, *R²* = .80, ƒ² = 0.03; small) 4. Post-test paranoia predicted by pre-test paranoia and groupXactive rejection (*p* <.01, *R*² = .80, ƒ² = 0.04; small) and by groupXpassive rejection (*p* <.01, *R²* = .80, ƒ² = 0.03; small). |
| Bullock et al. (2016) | 1. Significant interaction effect on state paranoia (*p* <.001, *ηᵨ²* = 0.77; large) and state anxiety (*p* <.001, *ηᵨ²* = 0.75; large); both increased in the negative condition and decreased in the positive condition. |
| Casanova et al. (1988) | 1. Main effect of impaired hearing on paranoia (*ps* <.001 - <.05, *ds*¹ 0.13 - 0.39; small), state anxiety (*p* <.05, *d*¹ = 0.83; large), mistrust and negative attribution (*p* <.001, *d¹* = 1.72; large) 2. Main effect of unfavourable feedback on paranoia subscales except hostility (*p*s <.01 - < .05, *d*s¹ 0.13 - 0.36; small), state anxiety (*p* < .05, *d*⁴ = 0.75; large), and mistrust and negative attribution (*p* <. 001, *d*¹ = 1.03; large) 3. No interaction effect *(p* > .15). |
| Cowles and Hogg (2019) | 1. Significant interaction effect of randomisation order (*p* = .036, *d*1 = 1.34; large): participants randomised to anxious condition first had significantly less paranoia distress after neutral condition. 2. Significant increases in paranoia (*p* = .001, *d* = 1.07; large) and anxiety (*p* < .001, *d* = 1.82; large) in anxious memory condition. 3. Significant decreases in paranoia (*p* = .029, *d* = 0.37; small) and anxiety (*p* = .011, *d* = 0.45; small) in neutral memory condition. 4. State anxiety significant predictor of state paranoia after anxious memory recall (*p* = .009). 5. Trait paranoia significant predictor of state paranoia after anxious memory recall (*p* = .03). |
| Foster et al. (2010) | 1. Significant reduction of worry (coefficient -10.00, *p* = .025) in intervention group compared to TAU, maintained at two month follow up 2. No significant reduction in GPTS ideation (-10.50, *p* = .255) or distress (-4.58, *p* = .285) 3. Significant associations between changes in worry and GPTS ideation at both follow-ups (*k* = .390, *p* = .018; *k* = .342, *p* = .038) and with GPTS distress at follow up 2 (*k* = .381, *p* = .021). |
| Franco et al. (2010) | 1. Significant between-groups differences at post-test in anxiety (*p* = .001, *d*¹ = 1.13; large), phobic anxiety (*p* <.05, *d*¹ = 0.75; medium), and paranoid ideation (*p* <.05, *d*¹ = 0.78; medium) 2. Significant reduction in experimental group anxiety (*p* = .001, *d* = 1.20; large), phobic anxiety (*p* <.05*, d* = 1.03; large), and paranoid ideation (*p* <.05, *d* = 1.04; large) from pre to post-test, and from pre-test to follow-up (anxiety: *p* < .01, *d* = 1.06; large; phobic anxiety: *p* <.05, *d* = 0.77; medium, and paranoid ideation: *p* <.05, *d* = 0.89; large) 3. No significant difference between post and follow up scores (all *p* > .102) |
| Freeman et al. (2015) | 1. Significant between-group differences in total paranoia (effect = 0.37, *p* = .037), state paranoia (effect = 5.98 *p* = .012), schizotypal questionnaire (effect = 2.14, *p* = .007) and anxiety (effect = 27.48, *p* = .001) at post-test: all increased in experimental condition 2. Partial mediation of anxiety, negative beliefs about others, depression (~40%) and negative beliefs about self (15%) on post-test paranoia. |
| Garety et al. (2015) | 1. Significant between-groups differences in post-test paranoia (effect size = -0.36, *p* = .028): scores decreased in experimental group 2. No post-test group differences in anxiety (effect size = -1.00, *p* = .874) 3. No mediation effects found when controlling for baseline scores. |
| Giusti et al. (2017) | 1. Significant interaction effect on anxiety (TAI; *p* < .01, *ηᵨ²* = 0.181; large, SAS; *p* <.01, *ηᵨ²*= 0.558; large) and paranoia (*p* < .05, *ηᵨ*²= 0.077; medium): all scores reduced in the experimental group at post-test 2. Significant baseline paranoiaXgroup effect on anxiety (SAS: *p* <.01, *ηᵨ*²= 0.632; large, TAI; *p* <.01, *ηᵨ²=* 0.202; large) and paranoia (*p* <.01, *ηᵨ*²= 0.546; large): the high paranoia subgroup in experimental condition showed the greatest reduction in scores. |
| Hou et al. (2014) | Significant between-groups differences in post-test anxiety (*p* <.001, *d*¹ = 1.93; large) and paranoid ideation (*p* = .09, *d*¹ = 0.35; small): scores lower in the experimental condition at post-test. |
| Isnanda et al. (2014) | 1. Significant effect of probability on paranoid comments during (*p* = .001, *d*¹ = 1.64; large) and after *(p* < .001, *d*¹ = 1.69; large) exposure 2. ProbabilityXcycle interaction effect on paranoid comments during exposure (*p* = .03, *d*¹ = .99; large): more comments were made in the short-vs-long cycle in low probability condition (*p* = .033, *d*¹ = .92; large) 3. No differences in type of paranoid thought (*p* = .28) 4. Between group differences in type of stressors (χ² (3) = 30.26; *p* <.001): snatches of conversation resulted in more paranoid comments than in the expressions and walking around conditions 5. ProbabilityXcycle interaction effect on anxiety *(p* = .010, *d*¹ = .85): more distress from short cycle in low-probability condition. |
| Müller et al. (2014) | Significant differences in paranoid ideation (*p* <.05, *d*⁴ = 0.69), anxiety (*p* <.01, *d⁴* = 0.79) and phobic anxiety (*p* <.05, *d*⁴ = 0.64) at 18 month follow up: experimental group scores reduced more than controls. |
| Newman-Taylor et al. (2018) | 1. Significant interaction effect on state paranoia (*F* (1,299) = 11.96, *p* = 0.001, *ηp²*= 0.04; small): scores in secure-imagery condition reduced at post-test (*p* < .001). 2. Significant interaction effect on state anxiety (*F* (1, 296) = 52.56, *p* <0.001, *ηp²*= 0.15; large): reduction in secure-imagery condition scores (*p* < 0.001) and increase in anxious-ambivalent condition scores (*p* < 0.001) at post-test. |
| Passini et al. (1977) | 1. Significant interaction effect on two anxiety measures (SAI; *p* <. 05, *d*¹ = 0.48; small, TAI; *p* <.05, *d*¹ = 0.71; medium): scores reduced in the experimental condition. No effect on the third measures (BPRS anxiety; *p* >.05) 2. Significant interaction effect on MMPI paranoia (*p* <.05, *d*¹ = 0.48; small) and BPRS suspiciousness (*p* <.05, *d*¹ = 0.49; small): scores reduced in the experimental condition. |
| Pourmohamadreza-Tajrishi et al. (2015) | 1. Significant differences in phobia (*p* <.001, *η*² = .48; large), paranoid thought (*p* <.001, *η*² = .03; small) and anxiety (*p* <.001, *η²* = .50; large) at post-test: experimental group scores lower than control. |
| Reeve et al. (2018) | 1. Significant increases in paranoia (*p* = .003, *d* = 0.39; small), anxiety (DASS; *p* < .001, *d* = 1.00; large), and worry (*p* = .005, *d* = 0.40; small) in restricted sleep condition at poat-test. 2. Significant interaction effect between baseline scores and effect of sleep condition on paranoia (*p* = .001): higher baseline score results in larger effect of sleep condition. 3. Effect of sleep on paranoia significantly mediated by anxiety (*p* = .014), depression (*p* = .001), stress (*p* = .002) and negative-other beliefs (*p* = .009). |
| Talakoub et al. (2012) | Significant within-group differences in anxiety (*p* =.001, *d*¹ = 1.04; large), phobic anxiety (*p* =.001, *d*¹ = 1.28; large) and paranoid ideation (*p* =.001, *d*¹ = 1.16; large) in experimental group pre to post manipulation. 2. No significant changes in control group (all *p* <.05). |
| Xu et al. (2016) | 1. Between-group differences in anxiety (*p* = .002, *d*¹ = 0.6; medium) and paranoia (*p* = .010, *d*¹ = 0.49; small) at post-test: experimental group scores lower than control. 2. Within-groups differences across all anxiety and paranoia measures in the experimental group (all *p* <.05): scores lower at post-test 3. No pre to post-test differences in control group scores. |
| ¹ *Effect size calculated using Thalheimer & Cook (2002)*  ² *Footnote “2” not employed as appears erroneously as a square-foot symbol in some instances*  ³ *Effect size calculated using Cohen (1992)*  ⁴ *Effect size calculated from www.psychometrica.de/effect\_size* | |

Total yield from search terms = 968

Identification

**Limiters applied** English language, academic journals, journal or article

Total = 643

**Minus duplicates (N = 165)**

Total = 477

Screening

**Not relevant from screen (N = 220)**

None of search terms B appearing in title or abstract (n = 96)

Not specified paranoid or persecutory delusion (n = 103)

Suspicion other than internal state (n = 20)

“Paranoid” as unrelated acronym (n = 1)

Total = 257

**Exclusion 1: Methodology (N = 155)**

Other quantitative design (n = 77)

Single level of manipulated variable (n = 36)

Not quantitative design (n = 42)

Total = 102

Eligibility

**Exclusion 2: Measures (N = 78)**

No paranoia measure (n = 9)

No anxiety measure (n = 22)

Both or either measure not used or analysed as separate construct at each time points (n = 48)

Total = 23

**Exclusion 3: Drug manipulation only (N = 4)**

Confirmed included = 19

Included

*Figure 1.* PRISMA flow diagram of the search and selection process.