Persecutory delusions: a cognitive perspective on understanding and treatment

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<u>**Personal View**</u>

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Abstract

A spectrum of severity of paranoia (unfounded thoughts that others are deliberately intending to cause harm) exists within the general population. This is unsurprising: deciding whether to trust or mistrust is a vital aspect of human cognition, but accurate judgement of others' intentions is challenging. The severest form of paranoia is persecutory delusions, when the ideas are held with strong conviction. This paper presents a distillation of a cognitive approach that is being translated into treatment for this major psychiatric problem. Persecutory delusions are viewed as threat beliefs, developed in the context of genetic and environmental risk, and maintained by several psychological processes including excessive worry, low self-confidence, intolerance of anxious affect and other internal anomalous experiences, reasoning biases, and the use of safety-seeking strategies. The clinical implication is that safety has to be relearned, by entering feared situations after reduction of the influence of the maintenance factors. An exciting area of development will be a clinical intervention science of how best to enhance learning of safety to counteract paranoia.

"Trust dies, mistrust blooms." Sophocles (1)

"He does not venture alone, for fear he should meet the devil, a thief, be sick; fears old women as witches, and every black dog or act he sees he suspecteth to be a devil, every person near him is maleficiated, every creature, all intent to harm him." Burton (2)

"But it is impossible to go through life without trust: that is to be imprisoned in the worst cell of all, oneself." Greene (3)

Trust is the foundation stone of communities; excessive mistrust a corrosive. Yet although every day each of us must decide whether or not to trust other people, this can be a difficult judgement. The level of threat we face varies by individual, time, and place; nonetheless, real threats from others exist and these must be anticipated and judicious precautions put in place.

The balance between trust and mistrust is often vicariously set by learning from those around us. But our innate levels of anxiety, the events that happen to us, and the inherent difficulties in decoding the intentions of others, mean that there is substantial individual variability in the accuracy of judgements concerning trust. When judgements are too far weighted to mistrust, then we are advancing along the paranoia spectrum.

The erroneous thought that others are deliberately intending to harm us is termed persecutory ideation (see Table 1). When such persecutory ideation is held with a high degree of certainty, we are experiencing persecutory delusions. Our contention is that all such paranoid thinking arises, in part, from normal cognitive processes concerning judgements of trust. Psychiatric research is still predominately focused on trying to explain the diagnostic category of schizophrenia, but the past fifteen years have seen a major advance in understanding the causes of paranoid thinking specifically. Increasingly, this knowledge is being translated into potentially much more efficacious treatment for those experiencing persecutory delusions in the context of psychiatric diagnoses such as schizophrenia. Notably, this work has originated from a clinical cognitive perspective. This paper will provide a distillation of a specific cognitive approach to persecutory delusions.

Table 1 about here

3

Conceptualising the phenomena: the paranoia spectrum

A clinical reality with face validity seems to have become obscured: experiences such as grandiosity, paranoia, hearing voices, thought disorder, and anhedonia are quite different. Yet the standard psychiatric view is that each is simply a possible symptom of a psychotic disorder such as schizophrenia. The diagnosis explains the symptoms, runs the logic. However, in a factor analysis of the psychiatric assessments of over 600 in-patients with a functional psychotic disorder, Peralta & Cuesta (5) 'concluded that the factor structure of psychotic symptoms is more complex than is generally acknowledged'. Peralta and Cuesta identified eleven different first-order factors corresponding to different psychotic symptoms (e.g. paranoia, hallucinations, poverty of speech). Such complexity has been repeatedly found (e.g. 6, 7). Rather than describe these phenomena as 'symptoms', it may well be better to consider them as individual psychotic experiences. Each has been found to have differing heritability (8). Each will require different explanation, notwithstanding that there are shared causal mechanisms across many different types of mental health problems. A focus on individual psychotic experiences also corresponds to clinical need, since it is these experiences that patients find troubling (e.g. feeling attacked, hearing upsetting voices). Paranoia is repeatedly identified as one of these individual psychotic experiences.

Paranoia is a term used widely but with varying meanings (9). It has been used, for example, to refer to all types of delusional thinking; to a distinct diagnosis; and to general suspiciousness (9). This has undoubtedly caused confusion. In this paper, the term paranoia is used to mean ideas of reference and persecution. However, the defining feature is persecutory ideation: unfounded ideas that harm is going to occur and that the persecutor has this deliberate intention (see Table 1). (Ideas of reference are a little less specific. Although they are most frequently the basis for persecutory elaborations, they can also serve as a foundation for grandiose ideas.) A spectrum of paranoia exists within the general population: many people have a few paranoid thoughts; a few have many (11). This is the same pattern we see in common emotional disorders such as anxiety and depression. Analysis of national epidemiological data indicates that there is a single paranoia dimension (12). Persecutory delusions are the extreme end of the dimension.

Persecutory delusions are a major psychiatric problem. Over 70% of patients presenting with a first episode of psychosis have a persecutory delusion (13); approximately half of patients with these delusions show levels of psychological well-being in the lowest 2% of the general

population (14); and psychiatric hospital admission is a common consequence (15). When individuals believe they are in imminent danger, being around other people becomes extremely difficult. Hence these delusions can lead to social withdrawal, exacerbation of emotional distress, and a much lower quality of life. Successful treatment, therefore, can produce numerous important benefits for patients. However, treatment that leads to total recovery is all too rare. Antipsychotic medication has effect sizes (standardised mean differences) varying between 0.33 and 0.88 (median=0.44) (16), and major side-effects, poor compliance, and residual problems are common. The effects on delusions of first generation cognitive-behavioural treatments when added to medication are typically a little lower (d= 0.36) (17). Moreover, service implementation of these therapies remains problematic (18). Consequently, what we see is a group with often very high levels of problems but showing treatment effects that are actually lower than those for conditions such as anxiety disorders (19). A radical improvement in treatment outcomes for patients with persecutory delusions is therefore urgently required.

A cognitive model of paranoia

Debates about delusions being caused by either one or two factors are out-dated. The complexity of causation in delusions is apparent in discussions with patients but also when the results of empirical studies are considered. Many contributory factors are implicated in persecutory delusions. It is most certainly not a matter of one or two causes. Indeed mental health disorders in general are typically the result of an interaction between multiple causes, and the same disorder can follow from varying combinations of causes. Thus each cause is an 'inus condition' (20) – 'an insufficient but non-redundant part of an unnecessary but sufficient condition.' A single cause therefore only increases the probability of a delusion occurring. And the defining feature of a causal factor - in the context of either the development or maintenance of a delusional belief - is that when altered it leads to a change in the delusion. How then does one choose which causes to focus upon? We highlight those that are:

- plausible mechanistically (and therefore likely to have strong connections);
- present in a large proportion of patients with persecutory delusions;
- potentially tractable;
- and the causal role has been tested by manipulation (in experimental and/or intervention studies).

The key psychological inroad into understanding persecutory delusions is to recognise them as threat beliefs (21) (see Figure 1). At the centre of the delusion is the belief that harm will occur from others. The individual believes that he or she is currently unsafe. Unlike threat beliefs in problems such as social anxiety where the fear is, for example, of rejection by others because of looking foolish, or panic disorder where the fear is, for example, of having a heart attack, in persecutory delusions the belief is that others *deliberately* intend to cause the harm. When the threat system has been activated, anxiety-related processes of threat anticipation are operative, while negative images of threat (e.g. being stabbed on the street) may also reinforce the belief (22). Consistent with this are studies that have shown using experience sampling methodology that negative affect precedes paranoia (23, 24) and, at the neurobiological level of explanation, amygdala hyperactivity occurring with paranoia (25).

Persecutory threat beliefs develop in the context of genetic and environmental risk. Zavos and colleagues (8) assessed paranoia dimensionally in five thousand adolescent twin pairs. They found that the relative contribution of genetic and environmental risk, even at the extreme end of paranoia scoring, was equivalent. The specific identification of genes with paranoia has barely begun (26). However, the contribution of environmental events such as physical abuse is clear and self-evident (e.g. 27), with the caveat that there may also be a degree of shared genetic propensity between particular life events and paranoia (gene-environment correlation) (28). Paranoia has also been linked to many other environmental factors including poverty, poor physical health, less perceived social support, stress, less social cohesion, cannabis use, and problem drinking (e.g. 29, 30).

But why do the threat beliefs persist when they are unfounded? Six processes are key (see Figure 1). First, worry brings implausible fearful ideas to mind, keeps them there, and exacerbates the distress. Patients with persecutory delusions show a worry thinking style comparable to patients with generalised anxiety disorder (31). Evidence shows a dose-response relationship between levels of worry and paranoia (32). Moreover, the presence of high worry predicts the persistence of persecutory delusions (33).

Second, negative self-beliefs, often developed in the context of adverse inter-personal experiences, mean that the individual feels inferior to others, different and apart, and hence vulnerable. Paranoia feeds on vulnerability. Three systematic reviews have highlighted that

negative self-beliefs are prevalent in paranoia (34, 35, 36). Causing a reduction in self-confidence in vulnerable individuals leads to an increase in paranoid thoughts (37, 38, 39).

Third, paranoia thrives when an individual is in a subjectively anomalous internal state: odd internal sensations and perceptions provoke fearful explanations. Most frequently, the high physiological arousal typically associated with anxiety is mistaken to indicate external threat. Dissociation is common too, and is exacerbated by bouts of worrying (40). In some instances aberrant salience may be misinterpreted (41), but, a much wider range of perceptual anomalies have consistently been linked with the occurrence of paranoid thinking (42) and schizophrenia more generally (e.g. 'basic symptoms'; 43). An experimental study with over one hundred individuals vulnerable to paranoia showed that cannabis causes a wide range of anomalous experiences and poorer working memory performance, but only the former led to the occurrence of paranoia (44).

Fourth, disrupted sleep (e.g. insomnia, hypersomnia, circadian rhythm disorder, nightmares) is likely to maintain paranoia via multiple routes. It will elevate negative emotion, mood dysregulation (45, 46, 47), and anomalous perceptions, and limit the cognitive resources available to revise initial interpretations of ambiguous situations. Patients also describe how the pervasive fatigue from poor sleep reduces their strength to cope with psychotic experiences (48). Certainly most patients with persecutory delusions are sleeping poorly (49). A review of 66 studies identifies disrupted sleep as a putative causal factor of psychotic experiences (50). The traditional view that sleep disturbances are a secondary epiphenomena in schizophrenia is now beginning to be turned on its head.

Fifth, reasoning biases prevent the processing of alternative explanations. Three quarters of patients with delusions do not report alternative explanations for the events they cite as evidence (51). A lack of 'belief flexibility' (that is, a willingness to generate and consider alternative explanations) locks patients into the delusional explanation of events. Belief inflexibility may be exacerbated by reduced data-gathering ('jumping to conclusions') (52, 53) and less use of analytic reasoning (54).

Finally, almost all patients try to reduce the persecutory threat by carrying out 'safety-seeking behaviours' (defensive strategies). But these reactions both prevent the processing of disconfirmatory evidence and enhance intolerance of negative affect. The concept of safety behaviours was developed in accounts of anxiety disorders (55), which showed how the problem with their use is the fact that patients attribute the absence of harm to their safety behaviours

rather than the inaccuracy of the threat ideation. Thus, disconfirmatory evidence is either not received or not processed. Habituation to anxiety is prevented. The most common type of safety behaviour used by patients with persecutory delusions is avoidance of situations (56). More subtle, but equally important, within-situation behaviours occur when in the places of perceived threat. For example, patients take steps to decrease their visibility, enhance their vigilance, and look out for escape routes. The higher the level of distress, the greater the use of safety behaviours (57).

These maintenance factors are all likely to be implicated in the original onset of the delusions. A dose-response relationship, rather than qualitative changes, explains shifts along the paranoia continuum. Typically, bi-directional relationships between the causes and paranoia become embedded. For instance, worry brings paranoid thoughts to mind, which, in turn, leads to greater levels of worry. The content of persecutory delusions is definitional. However, many of the maintenance factors in this cognitive account operate across a wide range of psychopathology. This is consistent with recent network approaches, which view disorders as arising from complex dynamic interactions of individual psychiatric symptoms and related processes that cut across traditional psychiatric classification systems (57, 58, 59). The commonalities should provide clinicians with greater confidence that psychosis is neither mysterious when compared to other conditions nor somehow qualitatively different.

This cognitive account, however, does differ from three alternative cognitive perspectives on paranoia. It is in direct contrast to an account that delusions are a defence to protect self-esteem against unconscious negative views of the self (60), instead resting on the conceptualisation that paranoia reflects and directly builds upon negative affect. We also do not consider that there are two distinct types of paranoia such as in the proposal of 'Poor me' and 'Bad me' (61). 'Poor me' paranoia was proposed to reflect a defence against negative emotions reaching consciousness and 'bad me' paranoia was proposed to be a direct reflection of conscious ideas about the self that are so extremely negative that the person believes they will be punished. This account of two types of paranoia with opposite causes is unconvincing. For instance, all the analyses of large epidemiological datasets indicate that there is just a single dimension of paranoia in the general population (12, 5, 6, 7, 8); the central test of the theory - a comparison of defence processes in patients with Poor Me compared to patients with Bad Me paranoia – has never been carried out; and a more parsimonious explanation is that this theory simply identifies one element of the content of paranoid thoughts (ideas about whether the persecution is deserved) that is tied to fluctuating levels of negative affect (similar to other aspects of the content such as ideas about

the power of the perpetrator). Finally, theory of mind difficulties have been the most researched psychological process in schizophrenia (62), since almost by definition the intentions of others are being misread in the content of paranoid thoughts, but it is not incorporated into our current account. This is because although there is strong evidence for theory of mind difficulties being present in patient groups, it is clear that these cognitive difficulties are most associated with negative symptoms and not paranoia (34, 63). The cognitive account presented has greater commonalities with views put forward by earlier theorists such as Arieti (64), Mednick (65), and McReynolds (66), who saw anxiety as central to the occurrence of delusions.

A translational treatment for persecutory delusions

From this cognitive perspective, the clinical goal becomes to enable the patient to form a strong belief concerning current safety, thereby allowing the persecutory threat belief to dissipate. The key clinical question is: how can patients re-learn safety?

In essence, the maintenance factors need to be removed and the patient must enter the threatening situations in order to learn directly that nothing bad occurs. The patient must learn to tolerate the high anxiety, associated physiological arousal, and other anomalous experiences, understanding that though they are uncomfortable they are not a sign of external threat. This learning of safety should allow a fundamental shift of attention away from activation of the negative valence system. Thus intervention starts to move from talk in the clinic room to direct, active, learning *in vivo*. Sessions are often spent, for example, going into shopping centres, or local streets, or initiating new activities, in order to build up beliefs of safety. (We have also often found value in talking with patients while outside simply walking, which can make the session both more comfortable and provide immediate environmental stimuli to discuss.) The focus is not on disproving past perceptions but in establishing knowledge of current safety.

How best to help patients relearn safety must become a research focus. It is not a trivial consequence that from this perspective clinical trials should recruit patients on the presence of having persecutory delusions, and that such delusions and related behaviours become the main outcome. (Similarly, too few trials have focussed solely upon hallucinations (67) or other individual psychotic experiences.) Translating the cognitive model outlined above, a series of studies of persistent persecutory delusions have shown the benefits of targeting the maintenance factors individually. These studies have used brief, manualised interventions presented one-on-one with a clinician in order to aid the theoretical interpretation, later dissemination, and the

building of a combined treatment. The strongest clinical test to date has been for reducing worry. A randomised controlled trial ('The Worry Intervention Trial') with 150 patients with persistent persecutory delusions had blind ratings and a 95% follow-up rate (68). Targeting worry, in just six sessions, significantly reduced both worry and the persecutory delusions (both effect sizes=0.5). A pilot randomised controlled trial ('The Self-Confidence Study') with 30 patients with persistent persecutory delusions, principally used techniques to enhance positive self beliefs in order to limit the effects of negative self beliefs (69). Treatment resulted in improved positive self beliefs (effect size= 1.0) and psychological well-being (effect size=1.2) and reductions in negative self-beliefs (effect size=0.24) and the delusions (effect size=0.6). An assessor-blind pilot randomised controlled trial ('The Better Sleep Trial') with 50 patients with persistent delusions and hallucinations showed that sleep can be substantially improved (effect size=1.9) and that there may be consequential benefits in levels of paranoia (effect size=0.2) and quality of life (effect size=0.5) (70). A trial with several thousand university students with insomnia is now underway that will have sufficient power to test definitively the relationship between sleep improvement and paranoia (71). Two randomised controlled studies have also shown the value of focussed individual work reducing reasoning biases in patients with delusions (72, 73). In a pilot clinical study with 31 patients with persistent delusions, the 'Thinking well' reasoning intervention led to a reduction in delusional conviction (effect size=0.6) compared to standard care (73). Finally, a recent study shows that testing the predictions of the persecutory threat beliefs by entering feared situations while dropping safety behaviours reduces the delusions to a much greater extent than exposure alone (effect size=1.3) (74).

Throughout these studies, treatment up-take has been remarkably high, which suggests that the approaches appear relevant and useful to patients. Patients desire help, for example, to reduce worry, feel more self-confident, sleep better, and to feel safer. The outcomes also indicate the potential of targeted brief approaches derived from the cognitive perspective but, of course, they are not without their limitations. Each is based on the assumption that the chosen intervention techniques principally target the mechanism of interest. Beyond this assumption, no study has then attempted to establish the temporal relationships of changes in the mechanism to changes in the delusions. Apart from the study of safety behaviours (74) and the proof of principle reasoning trial (72), the studies have not used an alternative psychological therapy control condition, thereby limiting the confidence with which one can identify the active treatment techniques. It must also be recognised that there are clear challenges in this clinical area. Patients' frequent demoralisation and hopelessness mean that clinicians must often work within a context where active engagement with treatment is difficult. The adverse life circumstances of many

patients; a background of severe social disadvantage; and the use of alcohol and illicit drugs further complicate the treatment picture. That said, although we should be realistic about the context of treatment, we should not lose sight of the fact that most patients can make real clinical progress.

From the start, our objective has been to achieve a much higher recovery rate for persecutory delusions, carefully building a new treatment out of evaluated individual components framed within a cognitive model. An initial feasibility evaluation has now taken place, combining the intervention elements in a new 20 session translational modular treatment called *The Feeling Safe Programme* (75). Based upon questionnaire assessments and a brief clinical interview, a menu of treatment options is provided for patients, who then choose their preferred treatment elements and the order of implementation (hence treatment is personalised and includes patient preference). Seven of the eleven patients with persistent delusions in the context of non-affective psychosis attending secondary mental health services who have taken part in the Feeling Safe Programme no longer met criteria for a delusion after treatment (75). A randomised controlled trial of the Feeling Safe Programme, improved in light of the lessons of the feasibility evaluation, against an attention control is now underway (Current Controlled Trials ISRCTN18705064). The range of modules offered in the programme target each of the maintenance factors in Figure 1: reducing worry, increasing self-confidence, improving sleep, reducing the impact of voices and other anomalous experiences, improving reasoning processes, and behavioural tests for reducing fear beliefs and relearning safety (while dropping safety-seeking behaviours). The treatment differs from first generation CBT for psychosis by: including substantial elements that have not been included in the original manuals (e.g. addressing the often complex and pervasive sleep dysfunction, using worry reduction methods, incorporating positive psychology techniques to develop positive beliefs about the self); treatment proceeding via achieving measured change in each targeted mechanism, one at a time, using a sustained approach; the highly manualised modular elements; the specific focus on persecutory delusions; and by the avoidance of overly complex formulations, instead using clear personalised explanations that contain an encouraging rationale for how change can occur.

One advantage of constructing a treatment in this way is that as new developments in understanding and treating paranoia become evident they can be readily incorporated (e.g. 76, 77, 78). All such advances must be targeted at helping to establish new beliefs about current safety. The new approach has been tested in patients with persistent delusions but arguably may show even greater efficacy in those at much earlier stages of problems, including those identified as

having at risk mental states (ARMS) for psychosis (79), since problems will be less long-standing and support networks more likely to be in place. How to achieve synergy between psychological and pharmacological approaches needs testing at a micro level of detail in tightly controlled experimental studies; for instance, the timing, type, and dose of medication could all moderate how much can be learned by patients when going back into a situation that they fear. A more dynamic and responsive pharmacological approach may be envisaged that varies depending on the mechanism being targeted and the psychological techniques being used, but this has never been tested. It is likely that our understanding of paranoia will be particularly enhanced by a developmental perspective on its occurrence (80); by the identification of factors shared with and differing from other mental health problems such as grandiosity (81), anxiety (82, 42), and hallucinations (27); by studying the paranoia spectrum across different diagnoses; by determining the societal factors influencing both trust and mistrust; and by assessing the overall predictive values of theoretical models. As we hope can be seen in the cognitive approach outlined above, future research must adopt an integrated perspective, combining analysis of the phenomenon under investigation with an understanding of causes, and using this as the basis for the development of treatment methods. In this way, the future years should see a step change in outcomes for patients with persecutory delusions.

Conflicts of interest

Daniel Freeman has written popular science, self-help, and academic books about paranoia with several publishers for which royalties are received. He has received funding from the National Institute of Health Research (NIHR), Medical Research Council (MRC), and Wellcome Trust to carry out treatment development studies on the topic.

Contributions

The paper was written by Daniel Freeman.

References

(1) Sophocles (401BC/2006). Introductions and Translations to the Plays of Sophocles and Euripides. Vol 1. (Trans H. Love). Newcastle: Cambridge Scholars Publishing.

(2) Burton, R. (1651/2001). The Anatomy of Melancholy (Ed. H. Jackson). New York: New York Review Books.

(3) Greene, G. (1943). The Ministry of Fear. London: Vintage.

(4) T.D. Cook, D.T. Campbell (1979). Quasi-Experimentation: Design and Analysis Issues for Field Settings. Rand-McNally, Chicago.

(5) Peralta, V. & Cuesta, M. J. (1999). Dimensional structure of psychotic symptoms: an item-level analysis of SAPS and SANS symptoms in psychotic disorders. Schizophrenia Research, 38, 13-26.

(6) Wigman, J.T.W., Vollebergh, W.A.M., Raaijmakers, Q.A.W., Iedema, J., van Dorsselaer, S., Ormel, J., Verhulst, F.C., & van Os, J. (2011). The structure of the extended psychosis phenotype in early adolescence - a cross-sample replication. Schizophrenia Bulletin, 37, 850-860.

(7) Peralta, V., Moreno-Izco, L., Calvo-Barrena, L, & Cuesta, M. (2013). The low- and higher-order factor structure of symptoms in patients with a first episode of psychosis. Schizophrenia Research, 147, 116-124.

(8) Zavos, H.M.S., Freeman, D., Haworth, C.M.A., McGuire, P., Plomin, R., Cardno, A.G., Ronald, A. (2014). Consistent etiology of severe, frequent psychotic experiences and milder, less frequent manifestations: A twin study of specific psychotic experiences in adolescence. JAMA Psychiatry, 71, 1049-1057.

(9) Freeman, D. & Garety, P.A. (2000). Comments on the content of persecutory delusions: Does the definition need clarification? British Journal of Clinical Psychology, 39, 407-414.

(10) Manschreck, T. & Petri, M. (1978). The paranoid syndrome. The Lancet, 2, 251-253.

(11) Freeman, D., Garety, P.A., Bebbington, P.E., Smith, B., Rollinson, R., Fowler, D., Kuipers, E., Ray, K., & Dunn, G., (2005). Psychological investigation of the structure of paranoia in a non-clinical population. British Journal of Psychiatry, 186, 427-435.

(12) Bebbington, P., McBride, O., Steel, C., Kuipers, E., Radovanovic, M., Brugha, T., Jenkins, R., Meltzer, H., & Freeman, D. (2013). The structure of paranoia in the general population. British Journal of Psychiatry, 202, 419-427.

(13) Coid, J., Ullrich, S., Kallis, C., Keers, R., Barker, D., Cowden, F., & Stamps, R. (2013). The relationship between delusions and violence. JAMA Psychiatry, 70, 465-471.

(14) Freeman, D., Startup, H., Dunn, G., Wingham, G., Cernis, E., Evans, N., Lister, R., Pugh, K., Cordwell, J., & Kingdon, D. (2014). Persecutory delusions and psychological well-being. Social Psychiatry and Psychiatric Epidemiology, 49, 1045-1050.

(15) Castle, D., Phelan, M., Wessely, S., & Murray, R. (1994). Which patients with non-affective functional psychosis are not admitted at first psychiatric contact? British J Psychiatry, 165, 101-106.

(16) Leucht, S., Cipriani, A., Spineli, L., Mavridis, D., Örey, D., Richter, F., Samara, M., Barbui, C., Engel, R., Geddes, J., Kissling, W., Stapf, M., Lässig, B., Salanti, G., & Davis, J. (2013). Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. The Lancet, 382, 951-962.

(17) van der Gaag, M., Valmaggia, L., & Smit, F. (2014). The effects of individually tailored formulation-based cognitive behavioural therapy in auditory hallucinations and delusions: a meta-analysis. Schizophrenia Research, 156, 30-37.

(18) Haddock, G., Eisner, E., Boone, C., Davies, G., Coogan, C., & Barrowclough, C. (2014). An investigation of the implementation of NICE-recommended CBT interventions for people with schizophrenia. Journal of Mental Health, 23, 162-165.

(19) Ehlers, A., Hackmann, A., Grey, N., Wild, J., Liness, S., Albert, I., Deale, A., Stott, R. & Clark, D. (2014). A randomized controlled trial of 7-day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. American Journal of Psychiatry, 171, 294-304.

(20) Mackie, J.L. (1974). The Cement of the Universe: A Study of Causation. Oxford: Oxford University Press.

(21) Freeman, D. (2007). Suspicious minds: the psychology of persecutory delusions. Clinical Psychology Review, 27, 45-457.

(22) Schulze, K., Freeman, D., Green, C., & Kuipers, E. (2013). Intrusive mental imagery in patients with persecutory delusions. Behaviour Research and Therapy, 51, 7-14.

(23) Ben-Zeev, D., Ellington, K., Swendsen, J. & Granholm, E. (2011). Examining a cognitive model of persecutory ideation in the daily life of people with schizophrenia: a computerized experience sampling study. Schizophrenia Bulletin, 37, 1248-1256.

(24) Thewissen, V., Bentall, R.P., Oorschot, M., à Campo, J., van Lierop, T., van Os, J., & Myin-Germeys, I. (2011). Emotions, self-esteem, and paranoid episodes: An experience sampling study. British Journal of Clinical Psychology, 50, 178-195.

(25) Pinkham, A., Liu, P., Lu, H., Kriegsman, M., Simpson, C., & Tamminga, C. (2015). Amygdala hyperactivity at rest in paranoid individuals with schizophrenia. American Journal of Psychiatry, 172, 784-792.

(26) Sieradzka, D., Power, R.A., Freeman, D., Cardno, A.D., McGuire, P., Plomin, R, Meaburn, E. L., Dudbridge, F., & Ronald A. (2014). Are genetic risk factors for psychosis also associated with dimension-specific psychotic experiences in adolescence? PlosOne. DOI: 10.1371/journal.pone.0094398

(27) Bentall, R., Wickham, S., Shevlin, M. & Varese, F. (2012). Do specific early-life adversities lead to specific symptoms of psychosis? A study from the 2007 Adult Psychiatric Morbidity Survey. Schizophrenia Bulletin, 38, 734-740.

(28) Shakoor, S., McGuire, P., Cardno, A., Freeman, D., Plomin, R., & Ronald, A. (2015). A shared genetic propensity underlies experiences of bullying victimization in late childhood and self-rated paranoid thinking in adolescence. Schizophrenia Bulletin, 41, 754-763.

(29) Kawachi, I., Kennedy, B., Lochner, K., Prothrow-Stith, D. (1997). Social capital, income inequality, and mortality. American Journal of Public Health, 87, 1491–1498.

(30) Freeman, D., McManus, S., Brugha, T., Meltzer, H., Jenkins, R., & Bebbington, P. (2011). Concomitants of paranoia in the general population. Psychological Medicine, 41, 923-936.

(31) Freeman, D. & Garety, P.A. (1999). Worry, worry processes and dimensions of delusions. Behavioural & Cognitive Psychotherapy, 27, 47-62.

(32) Freeman, D., Pugh, K., Vorontsova, N., Antley, A. & Slater, M. (2010). Testing the continuum of delusional beliefs: an experimental study using virtual reality. Journal of Abnormal Psychology, 119, 83-92.

(33) Startup, H., Freeman, D. & Garety, P.A. (2007). Persecutory delusions and catastrophic worry in psychosis: developing the understanding of delusion distress and persistence. Behaviour Research and Therapy, 45, 523-537.

(34) Garety, P. & Freeman, D. (2013). The past and future of delusion research: from the inexplicable to the treatable. British Journal of Psychiatry, 203, 327-333.

(35) Kesting, M. & Lincoln, T. (2013). The relevance of self-esteem and self-schemas to persecutory delusions. Comprehensive Psychiatry, 54, 766-789.

(36) Tiernan, B., Tracey, R., & Shannon, C. (2014). Paranoia and self-concepts in psychosis. Psychaitry Research, 30, 202-313.

(37) Freeman, D., Evans, N., Lister, R., Antley, A., Dunn, G., & Slater, M. (2014). Height, social comparison, and paranoia: an immersive virtual reality experimental study. Psychiatry Research, 218, 348-352.

(38) Atherton, S., Antley, A., Evans, N., Cernis, E., Lister, R., Dunn, G., Slater, M. & Freeman, D. (2014). Self-confidence and paranoia: an experimental study using an immersive virtual reality social situation. Behavioural and Cognitive Psychotherapy. 11th Nov [ePub ahead of print]

(39) Lincoln, T., Hohenhaus, F., & Hartmann, M. (2013). Can paranoid thoughts be reduced by targeting negative emotions and self-esteem? An experimental investigation of a brief compassion-focussed intervention. Cognitive Therapy and Research, 37, 390-402.

(40) Freeman, D., Startup, H., Dunn, G., Cernis, E., Wingham, G., Pugh, K., Cordwell, J., & Kingdon, D. (2013). The interaction of affective with psychotic processes: a test of the effects of worrying on working memory, jumping to conclusions, and anomalies of experience in patients with persecutory delusions. Journal of Psychiatric Research, 47, 1837-1842.

(41) Kapur, S. (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology. American Journal of Psychiatry, 160, 13-23.

(42) Freeman, D., Gittins, M., Pugh, K., Antley, A., Slater, M., & Dunn, G. (2008). What makes one person paranoid and another person anxious? The differential prediction of social anxiety and persecutory ideation in an experimental situation. Psychological Medicine, 38, 1121-1132.

(43) Schultze-Lutter, F., Klosterkötter, J., & Ruhrmann, S. (2014). Improving the clinical prediction of psychosis by combining ultra-high risk criteria and cognitive basic symptoms. Schizophrenia Research, 154, 100-106.

(44) Freeman, D., Dunn, G., Murray, R., Evans, N., Lister, R., Antley, A., Slater, M., Godlewska, B., Cornish, R., Williams, J., Di Simplicio, M., Igoumenou, A., Brenneisen, R., Tunbridge, E., Harrison, P., Harmer, C., Cowen, P., Morrison, P. (2015). How cannabis causes paranoia: Using the intravenous administration of Δ9-tetrahydrocannabinol (THC) to identify key cognitive mechanisms leading to paranoia. Schizophrenia Bulletin, 41, 391-399.

(45) Westermann, S. & Lincoln, T. (2011). Emotion regulation difficulties are relevant to persecutory ideation. Psychology and Psychotherapy, 84, 273-287.

(46) Marwaha, S., Broome, M., Bebbington, P., Kuipers, E., & Freeman, D. (2014). Mood instability and psychosis. Schizophrenia Bulletin, 40, 269-277.

(47) Lincoln, T., Hartmann, M., Köther, U., & Moritz, S. (2015). Do people with psychosis have specific difficulties regulating emotions? Clinical Psychology and Psychotherapy, 22, 637-646.

(48) Waite, F., Evans, N., Myers, E., Startup, H., Lister, R., Harvey, A. G., & Freeman, D. (2015). The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. Psychology and Psychotherapy. doi: 10.1111/papt.12073. [Epub ahead of print]

(49) Freeman, D., Pugh, K., Vorontsova, N. & Southgate, L. (2009). Insomnia and paranoia. Schizophrenia Research, 108, 280-284.

(50) Reeve, S., Sheaves, B. & Freeman, D. (2015). The role of sleep dysfunction in the occurrence of delusions and hallucinations. Clinical Psychology Review, 42, 96-115.

(51) Freeman, D., Garety, P.A. Fowler, D., Kuipers, E., Bebbington, P., Dunn, G. (2004). Why do people with delusions fail to choose more realistic explanations for their experiences? An empirical investigation. Journal of Consulting and Clinical Psychology, 72, 671-680.

(52) Dudley, R., Taylor, P., Wickham, S., & Hutton, P. (2015). Psychosis, delusions and the "jumping to conclusions" reasoning bias: a systematic review and meta-analysis. Schizophrenia Bulletin. Doi: 10.1093/schbul/sbv150

(53) Moritz, S. & Woodward, T. (2005). Jumping to conclusions in delusional and non-delusional schizophrenia patients. British Journal of Clinical Psychology, 44, 193-207.

(54) Freeman, D., Lister, R., & Evans, N. (2014). The use of intuitive and analytic reasoning styles by patients with persecutory delusions. Journal of Behavior Therapy and Experimental Psychiatry, 45, 454-458.

(55) Salkovskis, P.M. (1991). The importance of behaviour in the maintenance of anxiety and panic: a cognitive account. Behavioural Psychotherapy, 19, 6-19.

(56) Freeman, D., Garety, P., Kuipers, E., Fowler, D., Bebbington, P.E., & Dunn, G. (2007). Acting on persecutory delusions: the importance of safety seeking. Behaviour Research and Therapy, 45, 89-99.

(57) Borsboom, D. & Cramer, A. (2013). Network analysis: an integrative approach to the structure of psychopathology. Annual Review of Clinical Psychology, 9, 91-121.

(58) Hofmann, S. (2014). Towards a cognitive-behavioral classification system for mental disorders. Behaviour Therapy, 45, 576-587.

(59) van Os, J. (2015). The transdiagnostic dimension of psychosis: implications for psychiatric nosology and research. Shanghai Archives of Psychiatry, 27, 82-86.

(60) Bentall, R., Kinderman, P., & Kaney, S. (1994). The self, attributional processes and abnormal beliefs: towards a model of persecutory delusions. Behaviour Research and Therapy, 32, 331-341.

(61) Trower, P. & Chadwick, P. (1995). Pathways to defense of the self: a theory of two types of paranoia. Clinical Psychology: Science and Practice, 2, 263-278.

(62) Frith, C. (1992). The Cognitive Neuropsychology of Schizophrenia. LEA, Hove.

(63) Korver-Nieberg, N., Fett, A-K., Meijer, C., Koeter, M., Shergill, S., Haan, L., & Krabbendam, L. (2013). Theory of mind, insecure attachment and paranoia in adolescents with early psychosis and healthy controls. Australian and New Zealand Journal of Psychiatry, 47, 737-745.

(64) Arieti, S. (1974). Interpretation of Schizophrenia. 2nd Edition. London: Cosby, Lockwood, staples.

(65) Mednick, S. A. (1958). A learning theory approach to research in schizophrenia. Psychological Bulletin, 55, 316–327.

(66) McReynolds, P. (1960). Anxiety, perception and schizophrenia. In D. D. Jackson (Ed.), The Etiology of schizophrenia (pp. 248–292). New York: Basic Books.

(67) Birchwood, M., Michail, M., Meaden, A., Tarrier, N., Lewis, S., Wykes, T., Davies, L., Dunn, G., & Peters, E. (2014).. Cognitive behaviour therapy to prevent harmful compliance with command hallucinations (COMMAND). The Lancet Psychiatry, 1, 23-33.

(68) Freeman D, Dunn G, Startup H, Pugh K, Cordwell J, Mander H, Cernis, E., Wingham, G., Shirvell, K., & Kingdon, D. (2015) Effects of cognitive behaviour therapy for worry on persecutory delusions in patients with psychosis (WIT): a parallel, single-blind, randomised controlled trial with a mediation analysis. The Lancet Psychiatry, 2, 305-313.

(69) Freeman, D., Pugh, K., Dunn, G., Evans, N., Sheaves, B., Waite, F., Cernis, E., Lister, R., & Fowler, D. (2014). An early Phase II randomized controlled trial testing the effect on persecutory delusions of using CBT to reduce negative cognitions about the self. Schizophrenia Research, 160, 186-192.

(70) Freeman, D., Waite, F., Startup, H., Myers, E., Lister, E., McInerney, J., Harvey, A., Geddes, J., Zaiwalla, Z., Luengo-Fernandez, R., Foster, R., Clifton, L, & Yu, L-M. (2015). Efficacy of cognitive behavioural therapy for sleep improvement in patients with persistent delusions and hallucinations (BEST): a prospective, assessor-blind, randomised controlled pilot study. The Lancet Psychiatry, 2, 975-983.

(71) Freeman, D., Sheaves, B., Goodwin, G., Yu, L-M., Harrison, P., Emsley, R., Bostock, S., Foster, R., Wadekar, V., Hinds, C., & Espie, C. (2015). Effects of cognitive behavioural therapy for insomnia on the mental health of university students. Trials, 16, 236.

(72) Garety, P., Waller, H., Emsley, R., Jolley, S., Kuipers, E., Bebbington, P., Dunn, G., Fowler, D., Hardy, A., & Freeman, D. (2015). Cognitive mechanisms of change in delusions. Schizophrenia Bulletin, 41, 400-410.

(73) Waller H, Emsley R, Freeman D, Bebbington, P, Dunn G, Fowler D, Hardy A, Kuipers E and Garety P (2015) Thinking Well: A randomised controlled feasibility study of a new CBT

therapy targeting reasoning biases in people with distressing persecutory delusional beliefs. Journal of Behaviour Therapy and Experimental Psychiatry, 48, 82-89.

(74) Freeman, D., Bradley, J., Antley, A., Bourke, E., DeWeever, N., Evans, N., Černis, E., Sheaves, B., Waite, F., Dunn, G., Slater, M., & Clark, D. (in press). Virtual reality in the treatment of persecutory delusions: a randomised controlled experimental study testing how to reduce delusional conviction. British Journal of Psychiatry.

(75) Freeman, D., Bradley, J., Waite, F., Sheaves, B., DeWeever, N., Bourke, E., McInerney, J., Evans, N., Černis, E., Lister, R., Garety, P. & Dunn, G. (in press). Targeting recovery in persistent persecutory delusions: a proof of principle study of a new translational psychological treatment. Behavioural and Cognitive Psychotherapy.

(76) Hayward, M., Strauss, C., & Bogen-Johnston, L. (2014). Relating therapy for voices (the R2V study). Trials, 15, 325.

(77) van den Berg, D., de Bont, P., van der Vleugel, B., de Roos, C., de Jongh, A., Van Minnen, A., & van der Gaag, M. (2015). Prolonged exposure vs eye movement desensitization and reprocessing vs waiting list for posttraumatic stress disorder in patients with a psychotic disorder. JAMA Psychiatry, 72, 259-267.

(78) Lincoln, T., Hartmann, M., Köther, U., & Moritz, S. (2015). Dealing with feeling. Psychiatry Research, 228, 216-222.

(79) van der Gaag, M., Smit, F., Bechdolf, A., French, P., Linszen, D., Yung, A., McGorry, P., Cuijpers, P. (2013). Preventing a first episode of psychosis: a meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups. Schizophrenia Research, 149, 56-62.

(80) Wong, K., Freeman, D., & Hughes, C. (2014). Suspicious young minds: A study of two and a half thousand 8-14 year olds in the UK and Hong Kong. British Journal of Psychiatry, 205, 221-229.

(81) Garety, P., Gittins, M., Jolley, S., Bebbington, P., Dunn, G., Kuipers, E., Fowler, D. & Freeman, D. (2013). Differences in cognitive and emotional processes between persecutory and grandiose delusions. Schizophrenia Bulletin, 39, 629-639.

(82) Freeman, D., Thompson, C., Vorontsova, N., Dunn, G., Carter, L-A., Garety, P., Kuipers, E., Slater, M., Antley, A., Glucksman, E., & Ehlers, A. (2013). Paranoia and post-traumatic stress

disorder in the months after a physical assault: a longitudinal study examining shared and differential predictors. Psychological Medicine, 43, 2673-2684.

Table 1. Explanation of terms

Term	Description
Persecutory ideation	Unfounded (erroneous) cognitions of being targeted for harm, with ideation that comprises two main elements: the individual thinks that harm is occurring, or is going to occur, to him or her; the individual believes that the persecutor has the intention to cause harm.
Ideas of reference	Unfounded cognitions of being observed, followed, discussed, or the topic of messages or communications (e.g. in the media). The thoughts are distinguished form persecutory ideation by the absence of the attribution of intent to cause harm.
Paranoia	This is used to refer to the complete range of paranoia in the general population (i.e. the paranoia spectrum), including mistrust, suspiciousness, ideas of reference and persecution, and delusions. It is not simply used to refer to the psychiatric diagnosis paranoia (now called delusional disorder).
Persecutory delusions	The severe end of the paranoia spectrum, when the ideas are held with a strong conviction (at least 50% conviction) so that a belief is present. The beliefs vary along a number of dimensions, including the degree to which they are held, the amount of preoccupation, and the distress and impairment caused.
Cause	A manipulability view of causation (an interventionist-causal approach) is taken. If a factor is a cause of an event then altering the putative cause should lead to a change in the outcome of interest. As Cook and Campbell (4) describe: 'The paradigmatic assertion in causal relationships is that manipulation of a cause will result in the manipulation of an effect.'
Inus condition	'an insufficient but non-redundant part of an unnecessary but sufficient condition'. The classic example used to illustrate this is of a match as a causal factor to light a fire. The match is insufficient since other factors are needed to start a fire (e.g. oxygen, something to burn) but the match is non-redundant if these elements are in place. Together these elements combined are sufficient to start a fire. However it is an unnecessary condition since there are other ways to light a fire than

	using a match.
Effect size	An effect size provides an assessment of the strength of a relationship. Cohen's d is one of the most commonly used methods in treatment trials, providing an assessment of the standardised difference between two means. The change in the outcome for the intervention relative to the control group is divided by the pooled standard deviation of the whole sample. The effect size is often interpreted as small (0.2), medium (0.5) or large (0.8+).

Figure 1. The maintenance of persecutory delusions.